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PROLIFERATIVE RETINOPATHY IN DIABETES MELLITUS

REVIEW OF EIGHT HUNDRED FORTY-SEVEN CASES

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Clues to the relationship of proliferative retinopathy to diabetes were sought in the records of 44,249 patients with various forms of glycosuria. Data from the 847 cases of retinopathy so found showed that it most commonly developed in those diabetic persons with onset of disease early in life, but it was not a necessary consequence of diabetes in young patients. In those patients whose diabetes began before the 20th year, the average duration of diabetes before the discovery of proliferative retinopathy was 17.4 years, and none developed the condition in less than 8 years. It was usually the persons with onset of diabetes before 40 years of age, in whom insulin treatment and dietary management had been inadequate, who presented the characteristic neovascularization of the retina. There was also a definite association of proliferative retinopathy with diabetic nephropathy, and the latter was the predominant cause of death. Diabetic retinopathy is increasing in importance as a cause of blindness, and its prevention depends on early recognition and adequate treatment of the diabetes.

PROLIFERATIVE retinopathy in the adult has become almost pathognomonic of diabetes. It is the most characteristic evidence of malignant or severe diabetes, in contrast to mild forms of the disease. The association of retinitis proliferans with diabetic nephropathy (intercapillary glomerulosclerosis, Wilson-Kimmelstiel syndrome) and with premature atherosclerosis and arteriolosclerosis in the younger patients with severe diabetes is further evidence which identifies retinitis proliferans as one of the specific products of insulin deficiency and of the other metabolic defects which, taken together, constitute the disease diabetes mellitus.

The striking concentration of proliferative retinopathy in diabetic patients with onset of diabetes early in life should stimulate and guide research. Knowledge of the site and mode of action of insulin, as well as of the interrelations of insulin action with that of other hormones and metabolic regulators, is incomplete. The fact that the action of insulin varies in different tissues may be illustrated by the well-known differences in its effects in muscle, liver, and brain tissues. The possible effects of insulin deficiency in ocular tissues, especially the retina and retinal vessels, are, as yet, incompletely studied.

Incidence and Distribution

Incidence.—Even though a few cases of proliferative retinopathy were described as occurring in diabetic patients during the preinsulin era [1] and

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an association between proliferative retinopathy and diabetes was firmly established by Klien,[2] Hanum,[3] and Waite and Beetham,[4] this degenerative condition first became a serious problem in the treatment of diabetes during the last decade. The

Fig. 1.—Drawing of proliferative retinopathy occurring in young patient with long-term diabetes: *1*, few clusters of microaneurysms or punctate hemorrhages and slightly congested veins; *2*, discrete exudates; *3*, more severe venous varicosity; *4*, proliferative fibrous tissue and new vessel formation.

changes in the retina of diabetic persons are intimately related to a degenerative process affecting the small blood vessels, particularly the capillaries and venules. Proliferative retinopathy is defined as the type of retinopathy characterized by ophthalmoscopically observable, newly formed vessels and connective tissue in or in front of the retina (fig. 1).

The incidence of proliferative retinopathy has steadily increased. Waite and Beetham [4] found, prior to 1935, that, among 396 patients with diabetic retinopathy, 8% had proliferative retinopathy but that, in the years 1946 to 1956, among 2,103 patients with diabetic retinopathy 30% had proliferative retinopathy. Parallel to this increase in proliferative retinopathy is a substantial rise in blindness due to diabetes. In the United States, among 20,591 recipients of aid to the blind in 20 states 1.5% had diabetes. In Massachusetts, the highest rate of blindness due to diabetes was reported: 3.8%.[5] However, in the same state for the year ending Dec. 1, 1957, 18% of new persons on the register had diabetes.[6] Similar changes have been shown by other states.

Distribution of Proliferative Retinopathy.—Medical records in the Joslin Clinic from January, 1928, to Nov. 30, 1957, were screened (44,249 records, including patients with true diabetes and those with renal and nondiabetic glycosuria), and all cases of diabetic proliferative retinopathy, as established by a qualified ophthalmologist, were selected. The relationship of this lesion to the severity of diabetes and, more important, to the quality of treatment was the outstanding feature in the distribution of the condition among diabetic patients. Thus, 3,732 juvenile diabetics, with onset of disease from infancy to the 15th birthday, were treated at the Joslin Clinic up to Aug. 1, 1955. Of these 3,732 patients, 1,072 (28.7%) had survived 20 or more years and 879 were alive in 1956. In table 1 is an analysis of vascular lesions observed in these 879 patients, as presented by White in 1956.[7]

Retinitis proliferans was present in 28.7% of 158 patients between 20 and 29 years of age; this incidence increased to 53.1% in 527 patients between 30 and 39 years and to 58.4% in 176 patients between 40 and 49 years. The association with simple retinitis appears in the figures for "all types" of retinitis. Thus, in patients between 40 and 49 years of age, 58.4% had retinitis proliferans and, in addition, 29.6% had simple retinitis. Analyses of these patients' records indicate that delayed diagnosis of diabetes, lack of diabetic control, and failure to follow dietary treatment had characterized the group, as well as such complications as severe ketoacidosis and infections.

That retinitis proliferans is not a necessary consequence of diabetes in the young patient is indicated by two sets of data. First may be quoted the statement of Joslin and co-workers [8] that 34 patients with onset of diabetes between infancy and 15 years of age, out of 79 patients, have been winners of the Quarter Century Victory medal. The Quarter Century Victory medal is awarded to any diabetic patient who, after 25 years' duration of diabetes, is completely free from any retinitis or roentgenographic evidence of calcification in arteries and free from albuminuria and hypertension. Every one of these 79 patients had controlled his diabetes by testing the urine for sugar every day and altering his insulin dosage whenever necessary to control or prevent glycosuria. Second, data have been published from both the Joslin Clinic [8] and the University of Iowa [9] which indicate clearly that it is not merely the duration of diabetes but the quality and

TABLE 1.—*Total Incidence of Vascular Lesions by Age at First Observation of Each Lesion*

Age, Yr.	Albuminuria, %	Hypertension, %	Retinitis (All Types), %	Retinitis Proliferans, %	Calcified Arteries,* %
10-19	4.2	1.8	4.8	0	6.5
20-29	18.5	16.7	63.2	28.7	45.5
30-39	54.7	46.3	84.4	53.1	83.3
40-49	37.9	51.9	88.0	58.4	95.0

* Including patients with even minimal traces of calcium (visible in films only with hand lens.)

degree of the control of diabetes which will prevent or postpone retinitis. Thus, in 189 patients at the Joslin Clinic, with diabetes of 20 to 29 years' duration in every case, ophthalmological study of the eyes with studies of the arteries was reported. No patient with onset of diabetes after 20 years of age

was included. In those patients whose control of diabetes had been good throughout the period, 45% were entirely free from retinal hemorrhages or any retinitis at the end of the period, whereas, among 116 patients with poor control throughout that same period, marked or extreme retinitis was present in 36%. Indeed, in the experience at Joslin Clinic, no patient with excellent or good control of diabetes, immediate use of insulin at the onset of diabetes, continuous and good medical supervision, and daily testing of the urine to prevent glycosuria and hyperglycemia has been seen to have proliferative retinopathy.

Material and Methods

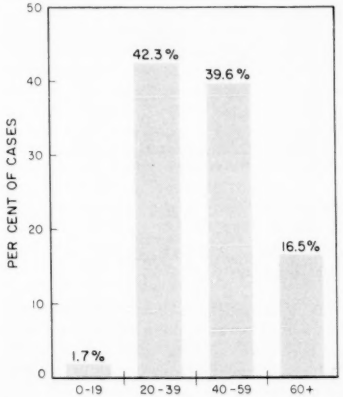
Proliferative retinopathy was defined as any retinal neovascularization. Every patient in this series, totaling 847, had a complete examination and report by a competent, certified ophthalmologist. The following information was extracted from each record: sex, age at diagnosis of diabetes, age at diagnosis of proliferative retinopathy, duration of diabetes, and insulin dosage at the time of diagnosis of proliferative retinopathy. In especially large groups the incidence of complete loss of vision, family incidence of diabetes, control of diabetes, and hypertension were evaluated.

The relationship of proliferative retinopathy to diabetic nephropathy was elucidated. Presumptive evidence of nephropathy was the presence of persistent albuminuria, with a level of at least 50 mg. per 100 ml., when this was not obviously due to other causes; edema; and hypertension (defined as persistent elevation of systolic blood pressure over 150 mm. Hg and diastolic blood pressure over 90 to 100 mm. Hg, according to age). Whenever the diagnosis was in doubt further kidney function tests were employed, e. g., urea clearance, phenolsulfonphthalein excretion, blood nonprotein nitrogen level, and urinary sediment. In addition, in a small group of patients with proliferative retinopathy, the capillary fragility, the vascular pattern of the conjunctival blood vessels, and paper electrophoretic fractionation of serum protein was determined; the results of these studies are reported elsewhere.[10] During the 30 year-period, 331 of the 847 patients with proliferative retinopathy died. In this group the prognosis as to the duration of life after the diagnosis of proliferative retinopathy had been made was established. In each of the fatal cases the causes of death were determined from death certificates or postmortem examinations.

Results

Incidence.—A total of 847 cases of proliferative retinopathy were recognized during the 30-year period up to Nov. 1, 1957. This number undoubtedly is an underestimation of the real incidence, because only a small portion of patients with long-term diabetes were regularly examined by an ophthalmologist. By examination of more than 400 diabetic persons with onset of disease before 45 years of age and duration varying from 10 to 25 years, we have found that for every patient with proliferative retinopathy approximately five had simple diabetic retinopathy. Many of these presumably have since developed neovascularization. This series included 379 males and 468 females, a sex distribution not far different from that for diabetic patients in general.[6]

Age at Time of Diagnosis.—Figure 2 presents the distribution of age at diagnosis of proliferative retinopathy. In more than 80% of patients, proliferative retinopathy was diagnosed before the age of 60. Proliferative retinopathy was found in only 14 (1.7%) of the diabetic patients under 20 years



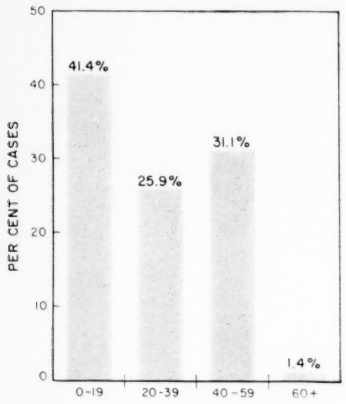
					TOTAL
MALE	5	187	147	40	379
FEMALE	9	171	188	100	468

Fig. 2.—Age at diagnosis of proliferative retinopathy in 847 diabetic patients.

of age. Thus, proliferative retinopathy is a condition predominantly recognized in young and middle-aged persons.

In figure 3 the distribution of age at diagnosis of diabetes in the 847 patients with proliferative retinopathy is presented. Of these patients, 351, or nearly 42% of the entire series, developed diabetes before the age of 20 years. This finding is in sharp contrast to the fact that only 13% of all diabetic persons have the onset of disease during these first two decades.[6] Diabetes was present before the age of 40 years in 68% of those with retinopathy; whereas in only 12 (1.4%) did diabetes, presumably beginning after the age of 60 years, lead to proliferative retinopathy.

Thus, proliferative retinopathy predominantly developed in the diabetic persons with onset of disease early in life. Proliferative retinopathy is extremely rare or may be nonexistent in patients with onset of diabetes after the age of 60, as our



	0-19	20-39	40-59	60+	TOTAL
MALE	182	107	87	3	379
FEMALE	169	113	177	9	468

Fig. 3.—Age at diagnosis of diabetes in 847 patients with proliferative retinopathy.

12 patients all had indefinite time of onset recorded. Thus, in these 12 patients, no urine or blood sugar tests had been performed for years before the discovery of glycosuria. Probably, onset of diabetes occurred long before the age of 60 years.

Duration of Diabetes.—In table 2 the average duration of diabetes before the recognition of proliferative retinopathy is given. Long duration of diabetes was a striking feature in the great majority of the patients. Thus, in those patients whose diabetes began before the 20th year, the average duration of diabetes before the discovery of proliferative

TABLE 2.—*Average Duration of Diabetes at Time of Diagnosis of Proliferative Retinopathy in 325 Patients*

Age at Diagnosis of Diabetes, Yr.	Av. Duration of Diabetes, Yr.	Variation in Duration, Yr.
0-19	17.4±4.2	8-28
20-39	17.8±6.6	3-29
40-59	10.2±6.2	1-28
60+	4.3±3.2	1-10

retinopathy was 17.4 years and none developed the condition in less than 8 years. For patients with diabetes beginning between the 20th and 40th year, the average duration of diabetes was 17.8 years. In six patients diabetes had been known for only three to six years, and these patients were all 38 or 39 years of age when the discovery was made. In patients over 50 years of age, a different picture was presented: a duration of less than eight years of diabetes was present in approximately one-half of the patients when proliferative retinopathy was found. However, in this older age group the difficulty of ascertaining the exact time of onset of diabetes has to be recognized.

Insulin Dosage.—In figure 4 the distribution of insulin requirement in patients with proliferative retinopathy is presented. The majority of patients required more than 25 international units daily, and most of these had onset of diabetes before the 45th year. It should be recognized that measurements of severity of diabetes dependent on insulin dosage are notably unreliable. Many temporary

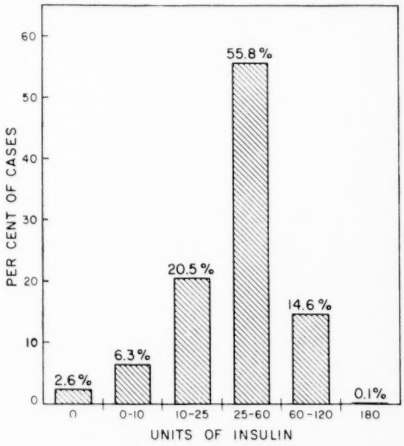


Fig. 4.—Insulin dosage (international units) in 847 diabetic patients with proliferative retinopathy.

factors, including improper diet, lack of physical exercise, infection, allergy, and renal status, would greatly modify the insulin requirement. Variations in dosage among our patients during their hospital stay often illustrated the decreasing insulin dosage with advancing renal failure and strict dietary rules. Many of the 249 patients who received from 0 to 25 units of insulin per day had formerly required a much higher dosage. In only 22 (2.6%) patients who had not received insulin did proliferative retinopathy develop, an illustration of delayed treatment.

Family Incidence of Diabetes.—The incidence of diabetes in the near relatives (grandparents, parents, uncles, aunts, and children) of 225 consecutive patients with proliferative retinopathy was found

to be 50.2%. This figure does not differ significantly from the average incidence of hereditary diabetes among all of our diabetics.[8]

Clinical Course.—It is usually the diabetic persons under 40 years of age, in whom insulin treatment has been delayed or inadequate and diet has been improper with resulting marked hyperglycemia, glycosuria, and periods of acidosis, who most frequently present neovascularization. Thus, in the vast majority of patients, a long duration of imperfectly controlled diabetes preceded the development of proliferative retinopathy. The capillary fragility index was often increased in our patients with proliferative retinopathy. Within months or years albuminuria usually developed. Frequently edema of the ankles occurred prior to albuminuria, but not infrequently a stage of nephrosis was already manifest at the time of diagnosis of proliferative retinopathy. The nephrosis usually responded well to treatment and the edema often improved. In the period of nephrosis albuminuria may be massive, blood cholesterol level elevated, and serum protein pattern markedly altered (albumin level decreased with elevation of alpha and beta globulin levels becoming more pronounced and irreversible with advancing diabetic nephropathy). In roughly 40% of the patients, albuminuria was present for some time prior to the discovery of proliferative retinopathy. However, in 60% hypertension was absent, and in fully one-third of the patients both albuminuria and hypertension were absent at the time of development of proliferative retinopathy and remained so for periods varying from a few months to several years.

TABLE 3.—*Incidence of Blindness in 206 Consecutive Cases of Proliferative Retinopathy*

Age at Diagnosis of Proliferative Retinopathy, Yr.	No. of Cases	Blindness, %
20-39	101	29.7
40-59	74	23.0
60+	31	29.0

With permanent urea retention, the clinical course was inevitably downward. Only exceptionally did patients survive from five to seven years after increased urea retention had been established. The duration of life after diagnosis of proliferative retinopathy varied widely. In 75 patients, this was less than 2 years, in 142 patients from 2 to 5 years, in 92 patients from 5 to 10 years, in 24 from 10 to 15 years; a total of 16 patients survived 15 years or more, and 9 of these are still living.

Infections of the feet and gangrene were rare in this group; amputation was required in only a small number of patients. The association with neuropathy was common.

In most of our patients, neovascularization was superimposed on features characteristic of simple retinopathy, i. e., microaneurysms, small punctate hemorrhages, and exudates. In many, neovascularization had developed insidiously, without evidence of sudden intravitreous hemorrhage. Venous changes in the retina, observed as increased fulness, with evidence of venous stasis or such venous alterations as localized bulges, sausage-shaped dilations, and beaded veins, were almost invariably present. The high incidence of venous change in patients with proliferative retinopathy contrasts with the finding in those with simple retinopathy, in whom venous changes were rarely encountered, especially in the older patients.

Table 3 presents the incidence of blindness in the last 206 consecutive patients with proliferative retinopathy. No blindness was found in any diabetic patient under the age of 20 years. In the three older age groups the incidence of blindness was approximately the same, about 25%. Glaucoma was recorded in 78 patients, and, in 25, hemorrhagic glaucoma required removal of an eye.

Cause of Death.—The cause of death in 331 patients with proliferative retinopathy is shown in table 4. The major cause of death was diabetic nephropathy with terminal uremia (44.5%). It occurred predominantly in the young diabetic patients (65.7%), to a lesser degree in the middle-aged group (46.4%), and in only 19% of the older patients. Arteriosclerotic heart disease, including coronary artery occlusion, was the terminal event in 37.4% of the patients. In contrast, this cause of death was most often observed in the older group (54.3%), even though an amazingly large number of young diabetic patients (under 39 years of age) also died from coronary occlusion (24.4%). Cerebral accidents were the cause of death in 20 patients and gangrene in 7. Coma was responsible for 3 deaths, hypoglycemia for 1, and miscellaneous causes (including pulmonary tuberculosis and cancer) for 29. No death occurred in a patient under 20 years of age.

TABLE 4.—*Cause of Death in 331 Patients with Proliferative Retinopathy*

	Age at Death, Yr.			Total	
	20-39	40-59	60+	No.	%
Nephropathy	86(65.7%)	39(46.4%)	22(19.0%)	147	44.5
Arteriosclerotic heart disease	32(24.4%)	29(34.5%)	63(54.3%)	124	37.4
Cerebral accident	2	6	12	20	6.1
Gangrene	1	1	5	7	2.1
Coma	1	1	1	3	0.9
Hypoglycemia	1	...	...	1	0.3
Miscellaneous	8	8	13	29	8.8
Total	131	84	116	331	

Comment

The analysis clearly demonstrates that proliferative retinopathy does not occur to the same degree in all diabetic patients with long-term disease, but predominantly in the young and middle-aged adults who have had diabetes for an average of approximately 17 years. The reason for the high

incidence in the younger age groups is not clear, but it is suggestive of a close relationship to the severity of diabetic aberration of metabolism.

Our data do not support the assumption in the literature that simple and proliferative diabetic retinopathy are two fundamentally different ocular disorders. In many of our patients, neovascularization was superimposed on features characteristic of simple retinopathy. Neither do our results suggest that diabetes in patients who develop proliferative retinopathy is different etiologically from that of diabetics with simple retinopathy.[9]

The hereditary background was quite similar in patients with or without proliferative retinopathy. However, the type of diabetes, in terms of the degree of severity, differed in patients with proliferative retinopathy in that their diabetes generally was labile, required relatively large doses of insulin, and was difficult to control. This relationship between the incidence of proliferative retinopathy and the juvenile type of diabetes provides evidence that the metabolic disturbance consequent on an insulin deficiency constitutes a major factor in the production of the retinal lesions. Further support for this contention is afforded by the recent reports [6] of retinopathy in patients with diabetes of hemochromatosis, of retinopathy and classic diabetic glomerulosclerosis in those with gross pancreatic fibrosis, and of retinopathy in the diabetic patients after pancreatectomy and relapsing pancreatitis.

Hypertension plays little or no role in the development of proliferative retinopathy, since the majority of our patients had no hypertension. Diabetic nephropathy often followed, rather than preceded, the onset of proliferative retinopathy.

Proliferative retinopathy developed often insidiously in the absence of an initial intravitreous hemorrhage and, thus, appeared to be formed by a primary new vessel proliferation. However, some cases of proliferative retinopathy may be ushered in as a profuse retinal hemorrhage perforating the internal limiting membrane. (Because neovascularization was occasionally observed in retinas showing but a few microaneurysms, it is incorrect in all cases to regard proliferative retinopathy as an advanced stage of simple retinopathy.) In agreement with others,[11] it has been our experience that venous alterations are prominent features in cases of diabetic retinopathy progressing to proliferative retinopathy. Venous congestion and stasis was often an outstanding finding in these patients, and, occasionally, the retinal alterations suggested a typical occlusion of one of the main venous branches. The pathogenesis of proliferative retinopathy may well be explained by the association with marked, prolonged venous stasis.

Even though the exact nature of the stimulus which governs the growth of newly formed blood vessels in the retina is not known, recent clinical and experimental studies [12] of retrolental fibroplasia (retinopathy of prematurity) have increased our knowledge as to this process. The retina has the highest rate of metabolism of any body tissue and demands an excellent blood supply.[13] Neovascularization takes place from the venules in an apparent response to factors associated with relative retinal anoxia. Ashton [14] found in pathological specimens of diabetic proliferative retinopathy that the neovascularizations were always associated with underlying areas of obliterated capillaries or obstructed veins. It is now believed that proliferative retinopathy primarily formed by an organizing intravitreous hemorrhage is relatively rare in patients with diabetes.[11] Each recurrent hemorrhage with scarring causes further retinal deterioration.

Because of the potential importance of the venous changes in the development of diabetic retinopathy, Ditzel and co-workers [15] recently studied the small vessels at a microscopic level in the bulbar conjunctiva. They found that venular dilation as part of a vascular response occurred frequently in young diabetics, to a lesser degree in middle-aged patients, and rarely in old diabetics, and therefore it shows a similar distribution in age as do both the retinal venous changes and the proliferative retinopathy. The venular dilation was often reversible, present for periods from the early onset of diabetes, and fluctuating with some relationship to the degree of diabetic metabolic disturbance.[16] The venular response, leading to stasis and slight exudation, was correlated with the presence and severity of retinopathy, indicating that reversible changes, particularly in the veins, play an important role in the development of the diabetic retinopathy.

When proliferative retinopathy has occurred, every effort should be made to control diabetes, to use insulin skillfully, and to maintain good nutrition. The effect of hypophysectomy has so far not been beneficial in our few patients with proliferative retinopathy in whom it has been employed. Our experience with proliferative retinopathy lends further support to the growing conviction that the sequelae of long-term diabetes are related to the degree of control maintained over the years. Therefore, the physician is obligated to plan treatment and to supervise management in such a way as to provide the best control attainable at the present time of hyperglycemia, glycosuria, and other abnormalities.

Summary and Conclusions

In an analysis of 847 consecutive cases of proliferative retinopathy among diabetic patients at the Joslin Clinic, no patient was found with this condition who had had good control of diabetes

with adequate diet and insulin therapy from the onset of the diabetes. The age at the onset of diabetes proved of greatest significance, in that diabetes developing early in life is severe, whereas diabetes developing late in life is, in general, mild.

Early diagnosis of diabetes and continuous control of diabetes may be of maximum importance in postponing and preventing proliferative retinitis, since many patients are now known to have survived diabetes with onset in childhood for periods of 20 to 30 years without any evidence of retinal hemorrhages when diabetic treatment has been adequate. The average duration of diabetes in this group at the time retinitis proliferans was recognized was 17.6 years, although it was impossible to correct the errors which are due to late or delayed diagnosis. The influence of sex and heredity appeared no different in diabetic patients with proliferative retinopathy than in those without.

The association of proliferative retinopathy and malignant diabetic nephropathy, or glomerulosclerosis of diabetes, is more intimate. Hypertension and albuminuria, although frequently absent at the onset, almost invariably appeared within months or years after the retinopathy. Causes of death were predominantly due to the diabetic nephropathy. Uremia was present in more than 50% of the patients. In the older group, although chronic glomerulosclerosis had been present, the terminal event was in many instances coronary occlusion.

The association of retinitis proliferans (proliferative retinopathy) with diabetic nephropathy and premature atherosclerosis in the young patient with severe diabetes further identifies this condition as one of the specific products of insulin deficiency and of the other metabolic defects which constitute the disease diabetes mellitus. The postponement or prevention of proliferative retinopathy is possible by intensified efforts to find diabetes early and to provide for its continuous adequate treatment by skillful use of insulin and of dietary measures.

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Drs. W. P. Beetham, J. Herbert Waite, Alfred Scott, John Hill, and Henry Mosher provided reports of ophthalmological examinations.

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THE FAMILY OF THE HANDICAPPED CHILD.—Handicapped children belong to emotionally healthy and mature parents and to neurotic and insecure parents. In other words, the typical parent of a handicapped child is, like most of us, a person who can take just so much and no more. There are many ways in which parents of handicapped children say "This is too much." Social workers and nurses have heard them all again and again. Let us hope that the ears of doctors, nurses, and social workers will be tuned to hear the true meaning of what is being said, and that their professional services will be broad enough and flexible enough to meet the needs. For if the families of handicapped children can be salvaged the children can probably be salvaged too.—E. S. Reid, Helping Parents of Handicapped Children, *Children*, January-February, 1958.

DIABETES IN A NEW ENGLAND TOWN

III. A COMPREHENSIVE BASELINE STUDY IN OXFORD, MASS.

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A group of 525 people, originally studied with reference to diabetes in 1946, were restudied in 1950 and 1953. In the original group there were 294 classified as normal, 70 as diabetic, and 161 as suspect because of postprandial hyperglycemia. In 1953, 292 subjects remained available for study, and it was possible to draw certain conclusions as to the characteristics of diabetic and prediabetic patients. Persons classified as suspect were eight times as likely as the normals to appear later in the diabetic group. Abnormalities of the eyes, heart, and great vessels were found much more frequently in the diabetic than in the other two groups. The predictive value of comprehensive physical examinations was evident, and it appeared likely that further studies of this sort may yield hints as to prophylaxis against diabetes and its complications.

In 1946, a survey to determine the prevalence of diabetes mellitus in an American community was conducted in Oxford, Mass.[1] The survey findings indicated a diabetes prevalence of 1.7% and suggested the estimate of one million known and one million unknown cases of diabetes in the United States. This estimate of diabetes prevalence has since become the basis for nationwide detection programs.[2] A follow-up study, in 1950,[3] confirmed the previous findings and added the information that persons with "a little sugar in the urine" or blood sugar levels "a little higher than normal" developed diabetes eight times oftener than those with normal blood sugar levels (14.4% as compared to 1.8%). The 1950 investigations further indicated that a more comprehensive follow-up study was necessary to bridge the gaps in available knowledge of detection, diagnosis, onset, and progress of complications of the disease. Therefore, in 1953, the present study was undertaken to establish a base line for long-term epidemiologic studies.

Study Groups

Three groups of persons from the original 1946 Oxford Study [1] were selected for long-term follow-up according to the following criteria:

Diabetic Group.—Persons were diagnosed as having diabetes who repeatedly had one-to-two-hour postprandial venous blood sugar levels of more than 169 mg. of sugar per 100 ml. of blood, as determined by the Folin-Wu method, with glycosuria, or capillary blood sugar levels in excess of 199 mg. per 100 ml., as determined by the Folin-Malmros method, with glycosuria. Also included in this group were persons who had been previously given, by their physicians, a diagnosis of the disease.

Blood Sugar Suspect Group.—Persons were classified as blood sugar suspects who had one-to-two-hour postprandial venous blood sugar levels between 140 mg. per 100 ml. and 169 mg. per 100 ml. (Folin-Wu method) or capillary values between 170 and 199 mg. per 100 ml. (Folin-Malmros method), with or without glycosuria.

Normal Control Group.—A normal control group was selected from those persons with one-to-two-hour postprandial venous blood sugar levels less than 140 mg. per 100 ml. or capillary blood sugar levels less than 170 mg. per 100 ml., without glycosuria. The group was randomly selected from age and sex strata similar to those of the blood sugar suspects.

The figure shows the transition of these three groups from 1946 to the present study of 1953 and shows what happened to the original 525 persons selected and classified in the 1946 study. In addition to the 292 persons indicated for 1953 in the figure, 15 persons from the general population of Oxford were included. They were persons who had been given a diagnosis of diabetes by their private physicians and who were referred to our epidemiologic study in the interim period between 1950 and 1953. The diagnoses were confirmed by our laboratory.

For the purpose of this base-line study, the blood sugar suspect group and normal control group of 1953 were combined and designated as "nondiabetic." The total of 307 persons available for study, therefore, comprised 72 diabetic and 235 nondiabetic individuals. Eight persons with questionable diabetes were conservatively classified in the nondiabetic group.

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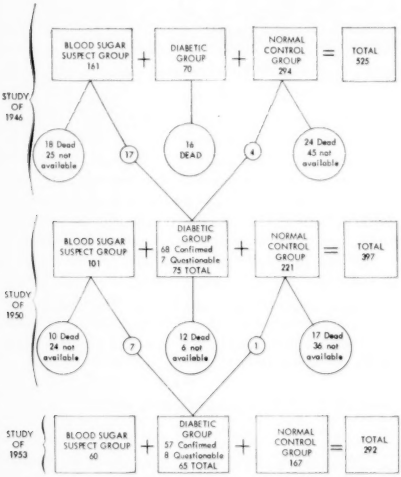
Method

The study in 1953 was broadened to include a history; physical examination; ophthalmological examination; retinal photographs; x-ray studies of the chest, pelvis, and extremities; and a 12-lead electrocardiogram. The laboratory work consisted of routine postprandial blood sugar determinations and glucose tolerance tests, when indicated; urine sugar and albumin tests; and determinations of blood serum cholesterol and lipid values. Periodic follow-up examinations have been made throughout the length of the study.

Preliminary Background.—The purpose of the comprehensive examinations in this study was to compare abnormalities in the diabetic and nondiabetic groups and also to establish a base line from which later studies on the same groups may be evaluated. As a preliminary background to the pathological results, a tabular summary of age, sex, heredity, and weight data is presented.



Transition of original Oxford study groups. Total of 292 does not include 15 diabetic persons referred to this present study from other sources.

Age and Sex: Of the 72 diabetic persons who met our criteria in 1953, 38 are males and 34 are females. They are an older group than the 235 nondiabetic persons; 26.4% are 65 years and over, as compared with 16.2% of the nondiabetic group; 59.7% are in the age group 45-64, as compared with 41.7% of the nondiabetic group (table 1). The age factor has been considered in the pathological findings studied for the two groups.

Heredity: Of the diabetic group, 43.1% reported one or more relatives with diabetes in the immediate family (parents, siblings, or children), and an additional 19.4% reported other blood relatives with diabetes (grandparents, aunts and uncles, or other). The 62.5% positive history in the diabetic group compares with 21.7% in the nondiabetic group (14.0% in the immediate family and an additional 7.7% with other blood relatives) (table 2).

TABLE 1.—*Age and Sex Distribution of Individuals Studied, by Classification, 1953*

Age, Yr.	Diabetics Male, No.	Diabetics Female, No.	Diabetics Total	Diabetics %	Nondiabetics Male, No.	Nondiabetics Female, No.	Nondiabetics Total	Nondiabetics %
<25	0	1	1	1.4	7	20	27	11.5
25-34	1	3	4	5.6	10	16	26	11.0
35-44	3	2	5	6.9	25	21	46	19.6
45-54	5	9	14	19.4	30	23	53	22.6
55-64	19	10	29	40.3	23	22	45	19.1
>65	10	9	19	26.4	23	15	38	16.2
Total	38	34	72	100.0	118	117	235	100.0

Overweight: On the basis of weight in 1953, the percentage of overweight diabetic males is about the same as in nondiabetic males: 34.3% compared with 32.5%. The percentage of overweight diabetic females is greater (46.6%) than nondiabetic females (34.5%). The difference is marked only for those aged 45 to 54 years.

On the basis of weight prior to 1953, 70% of diabetic males gave a history of previous overweight as compared with 47.9% of nondiabetic males. The percentage is greater for every age group 45 years and over. There was a history of overweight in 80% of diabetic females as compared with 52% in nondiabetic females. The differences, in general, hold for each age group.[4]

Pathological Differences Between Groups.—Through detailed physical and laboratory examinations it was hoped that pathological differences between the diabetic and nondiabetic groups could be discerned and defined. The results obtained from examinations of the skin, eyes, heart, and blood vessels are presented.

TABLE 2.—*Family History of Diabetes, by Classification, 1953*

History of Diabetes	Diabetics No.	Diabetics %	Nondiabetics No.	Nondiabetics %
No family history	27	37.5	184	78.3
Family history	45	62.5	51	21.7
Immediate family	31	43.1	33	14.0
Other relatives than immediate family	14	19.4	18	7.7
Total	72	100.0	235	100.0

Skin: Skin abnormalities and infections were not significantly different between the two groups, confirming clinical observations.

Eyes: Sixty-five (90%) of the diabetic persons and 201 (86%) of the nondiabetic persons had comprehensive ophthalmological examinations which included detection of retinal lesions, i. e.,

punctate and flame hemorrhages, cotton-wool and yellowish exudates and retinitis proliferans, vascular sclerosis of retinal vessels, and cataracts and blindness. Table 3, which summarizes the findings for both groups, shows a significant difference (at the level p=0.99) in retinal lesions between the diabetic and nondiabetic person. It is observed that the abnormalities are not associated necessarily with old age but occur with distressing frequency in the younger (25-44 years) and the middle-aged (45-64 years) diabetic individuals. Three blind diabetic persons were found in the 45-64 year age group, while there were no blind persons in the nondiabetic group. The evidence found under this category becomes increasingly significant when it is observed that these abnormalities are almost nonexistent among the nondiabetics.

Vascular sclerosis of the retinal vessels occurs with marked frequency in both the diabetic and the nondiabetic. The data indicate, however, that this abnormality may be associated with age, since the 81% and 73% of the diabetics and nondiabetics, respectively, thus afflicted are aged 45 years and over.

two groups in regard to the abnormalities of tortuous great vessels are questionable, while elongation of the aortic knob and widened aorta are more pronounced among the diabetics in the 25-44 and 45-64 year age groups.

X-ray of the Chest, Pelvic, and Leg Vessels.—Calcifications of the vessels of the chest, pelvis, and legs were not uncommon in both groups (table 5). They were, however, more marked among the diabetics and were found in 73.3% aged 25 and over as compared with 46.2% in nondiabetics. The only age group in which a marked difference occurs is the 45-64 year age group. Here the percentage of diabetics with calcification is 76.3% as compared with 55.2% in nondiabetics. In the younger diabetics (25-44 years) calcifications were no more marked than in the normal group. For those aged 65 and over, calcifications were almost universal.

The site of calcification occurred almost equally in the chest, pelvis, and leg vessels in the diabetics. Increased vascular damage in the diabetics is further demonstrated by the fact that three had suffered limb amputations and one had had bilateral midthigh amputations.

TABLE 3.—*Findings of Eye Examinations, by Age, Type, and Classification, 1953*

Age, Yr.	Diabetics, No.	Nondiabetics, No.	Retinal Lesions, %*		Vascular Sclerosis of Retinal Vessels, %		Cataracts, %	
			Diabetics	Nondiabetics	Diabetics	Nondiabetics	Diabetics	Nondiabetics
25-44	6	70	16.7	0	0	0	0	0
45-64	41	86	24.4	1.0	73.2	60.7	12.2	6.3
≥65	18	35	16.7	5.7	100.0	91.4	72.2	34.3
Total	65	201	21.5	1.5	78.8	47.8	27.7	9.0
≥45	59	131	22.0	2.3	81.3	73.3	30.5	13.7

* Includes punctate and flame hemorrhages, yellowish and cotton-wool exudates, and retinitis proliferans.

TABLE 4.—*X-ray Findings of the Heart and Great Vessels by Age, Type, and Classification, 1953*

Age, Yr.	Diabetics, No.	Nondiabetics, No.	Left Ventricular Hypertrophy, %		Tortuous Great Vessels, %		Other Great Vessels, %*	
			Diabetics	Nondiabetics	Diabetics	Nondiabetics	Diabetics	Nondiabetics
25-44	8	68	12.5	0	0	0	12.5	1.5
45-64	38	86	23.7	6.3	7.9	2.1	55.3	29.2
≥65	14	32	35.7	25.0	7.1	15.6	78.6	65.6
Total	60	186	25.0	7.1	6.7	3.6	55.0	25.5
≥45	52	118	26.9	10.9	7.7	5.5	61.5	38.3

* Aortic knob elongated, aorta widened and elongated.

Cataracts, in our series, are found to exist more frequently in diabetics, irrespective of age. This is a finding known to have been questioned as a result of analyses made by Waite and Beetham [5] in 1935.

X-ray of the Heart and Great Vessels.—The abnormality of left ventricular hypertrophy appeared to be more frequent among the diabetics x-rayed than among the nondiabetics. Of the diabetics aged 45 and over, 26.9% showed some irregularities while only 10.9% of the nondiabetics in this age group had similar defects (table 4). Differences between the

Other Characteristics of the Diabetic Group.—Other characteristics of the diabetic patients also were studied.

Medical Visits: Approximately 21% of the diabetics who had had the disease for more than one year had not seen a physician within a year. Thirty-three per cent had made one or two visits, while 28% had been under close supervision with six medical visits or more yearly. The percentage of nondiabetics who had not seen their physician was 38.3, considerably greater than that of the diabetics. While many of the diabetics are apparently not

frequently examined, the number of their medical visits is still greater than that of nondiabetics in the community.

Insulin Administration and Urine Testing: Thirty-eight of the 72 diabetics (53%) were taking from 10 to 70 units of insulin daily while 34 (47%) were taking no insulin at all. The persistently elevated blood sugar levels of the latter group would seem to indicate that these individuals should be considered for a more restricted dietary regimen or the addition of some kind of insulin schedule.

Forty-eight per cent of the diabetic group checked their urines regularly, 12% tested it infrequently, and the remainder not at all.

Birth Weights and Pregnancies: Of 23 diabetic females over age 40, 47.8% gave a history of one pregnancy or more resulting in a baby with birth weight of 10 lb. or greater. Seventy per cent of these 23 females had four pregnancies or more. In the nondiabetic group, 20% of 25 females over age 40 reported one or more pregnancy with baby birth weight of 10 lb. or more. Only 28% of these 25 females had four pregnancies or more. The evidence seems to indicate that more diabetic women give birth to large babies than do nondiabetic women. This is consistent with the findings of Hoet,[6] Moss and Mulholland,[7] and Jackson.[8]

TABLE 5.—*X-ray Findings of Calcification of the Chest, Pelvic, and Leg Vessels, by Age and Classification, 1953*

Age, Yr.	Diabetics, No.	Nondiabetics, No.	Chest Vessels, %		Leg Vessels, %		Pelvic Vessels, %		Any of These Vessels, %	
			Diabetics	Nondiabetics	Diabetics	Nondiabetics	Diabetics	Nondiabetics	Diabetics	Nondiabetics
25-44	8	68	0	0	12.5	10.3	12.5	4.4	12.5	11.8
45-64	38	96	55.3	31.3	63.2	37.5	57.9	13.5	76.3	55.2
>65	14	31	100.0	87.1	64.3	74.2	50.0	58.1	100.0	93.5
Total	60	195	58.3	29.2	56.7	33.8	50.0	17.4	73.3	46.2
>45	52	127	67.3	44.9	63.5	46.5	55.8	24.4	82.7	64.6

Comment

The findings in this phase of the Oxford study are important to the practicing physician because this study group is not a hospital or selected clinical population but consists of a diabetic population in a typical community setting. The findings therefore reflect varying degrees of control.

In contrast to the usual findings in medical literature, results of this study show that males are just as likely to have diabetes mellitus as females and that, while most known diabetics are past middle age, the condition is found in all age groups. These data also indicate that the diabetic has three times as many relatives who have diabetes as compared with the nondiabetic and that about two-thirds of the diabetics have one known diabetic relative or more.

From the data presented, it is evident that the family physician has an opportunity to practice health education as well as preventive medicine, because the average diabetic sees his doctor far more frequently than the average nondiabetic. Particular attention to eyeground examinations and electrocardiograms will provide the examiner with an accurate appraisal of the onset and progress of accompanying complications, such as retinopathy and changes consistent with early arteriosclerotic heart disease.

To the physician and his diabetic patient the future picture is a serious one. The natural history of diabetes indicates that, in the majority of cases, more rapid and extensive deterioration is likely with increased duration of the disease. It is a strange paradox that, in spite of increasing medical knowledge about diabetes mellitus and with almost positive means of diagnosis available, this chronic disease frequently remains undiagnosed and the victims untreated. Even when the disease is diagnosed and the patients are treated, its complications continue to be a source of disability to the patient and an increasing problem to the physician, often imposing a heavy socioeconomic burden on the patient's family and community.

The data presented suggest that definitive studies are needed to identify factors influencing the onset and progress of complications due to diabetes and to relate prognosis to varying degrees of control as influenced by insulin, weight, and diet. This concept was stated succinctly by Hardin and associates [9]: "The question of whether retinopathy and other degenerative diseases accompanying diabetes may be prevented or delayed by properly ordered treatment has been the subject of much investigation without a universally accepted decision. Probably the answer will not be achieved until the pathologic physiology of the degenerative lesions is completely understood and the causative factors are clearly related to their effects."

Summary

The status of the Oxford study groups of 1946-1947 has been reviewed after seven years. Despite the attrition of time and migration, the group with diabetes increases as persons in the blood sugar suspect group develop diabetes eight times faster than the normal control group. Results of the comprehensive physical examinations of the diabetic group and the nondiabetic group comprising the blood sugar suspect and normal control groups have been studied. Abnormalities are significantly more frequent in the diabetic group in comparison with the nondiabetic group, particularly in the eyes,

heart, and great vessels. The study serves to establish a base line and points to a need for future comparative evaluations where pathological findings may be correlated with degrees of control.

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LONG-TERM ANTICOAGULANT THERAPY IN CORONARY DISEASE

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An attempt has been made to evaluate the effectiveness of continuing the administration of anticoagulants over a period of years in the treatment of coronary heart disease. In a series of 521 patients there was a group of 408 with myocardial infarction, within which it was possible to make comparisons between 268 patients who kept up the anticoagulant treatment and 140 (pseudocontrols) who discontinued such treatment after three months to 10 years. Mortalities at both the 5-year and 10-year epochs were higher for the pseudocontrols (29 and 36%) than for those who continued the treatment (21 and 25%). The 5-year and 10-year mortality figures in the series available in the literature in which anticoagulants were not given (true controls) are 44 and 68% respectively. The conclusion that anticoagulant therapy improved the prognosis for the patient was corroborated by other comparisons within this series as well as comparisons with data published by other investigators. Anticoagulants in the dosages here used caused 58 minor and several rather severe hemorrhagic episodes but no fatalities.

Anticoagulant therapy in acute myocardial infarction is now well established, according to most authorities on the subject. Long-term therapy after the acute attack requires accumulation of statistics over a long period of years to make any conclusions valid. This is not an easy matter to evaluate, because there are countless variables entering into the natural history of these cases of coronary artery disease. The information available would seem to show that patients given long-term treatment are favorably affected.

Review of Literature

In the last few years, reports have been appearing in the literature on experiences with anticoagulants in the long-term treatment of coronary disease. In March, 1954, Nichol and co-workers [1] reported 295 patients with coronary disease on long-term anticoagulant therapy. The duration of treatment in this series ranged from three months to seven years. To summarize their results, in these 295 patients there were 41 deaths (13.8%) and 7 recurrences, while in the control group of 110 patients (after anticoagulant therapy was stopped) there were 37 deaths (33%) and 14 recurrences.

In April, 1955, Foley and co-workers [2] reported on 300 outpatients with myocardial infarction treated with long-term anticoagulant therapy. They summarized 23 cases as follows: In 11 patients who had had two or more episodes before therapy and who

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were not given anticoagulant therapy, over a period of 587 months there were 49 thromboembolic episodes (including 30 instances of myocardial infarction and 10 of pulmonary embolism); when anticoagulants were given, over a period of 393 months there were 3 thromboembolic episodes. In 12 patients who had had one episode and who were not given anticoagulant therapy, over a period of 41 months there were 12 thrombembolic episodes; when anticoagulants were given, over a period of 554 months there was only one episode.

Also in 1955, Suzman and associates [4] reported on 82 cases treated with anticoagulants for periods of 3 to 76 months after coronary thrombosis. We have summarized their results as follows: In the long-term group, the mortality was 7.3% and there were 7 recurrences (8%); in the control group, the mortality was 33% and there were 24 recurrences (27%). In patients with severe disease who were given long-term therapy, the mortality was 9% and there were 7 recurrences; in the control patients with severe disease, the mortality was 46.7% and there were 21 recurrences. The mortality was 14.3% before therapy was started in patients with severe recurrent disease; it was 66% in the control patients with severe recurrent disease.

In 1956, Keyes and co-workers [4] reported the following mortality in connection with long-term anticoagulant therapy after myocardial infarction: After one year had elapsed, in control patients with a single episode the rate was 16.1% and in those with recurrent disease it was 31.2%, while in patients given anticoagulants the rates were 4.2 and 8.0% respectively. After two years, in control patients with a single episode the rate was 27.9% and in those with recurrent disease it was 39.6%, while in patients given anticoagulants the rates were 5.6 and 8.0%. After three years, in control patients with a single episode the rate was 31.7% and in those with recurrent disease it was 52.1%, while in patients given anticoagulants the rates were 8.4 and 10.0%. After four years, in control patients with a single episode the rate was 41.4% and in those with recurrent disease it was 62.5%, while in patients given anticoagulants the rates were 8.4 and 12.0%.

In their series, the single infarction group consisted of 186 controls and 71 treated patients. In the recurrent infarction group there were 48 controls and 50 treated patients. The period of treatment ranged from six months to five years. These workers found the death rate in the group with single infarction to be three times greater when anticoagulants were not given. They also found that in the recurrent infarction group the death rate was five times greater without anticoagulant therapy.

Manchester,[5] in December, 1957, reported an interesting study on a group of patients given long-term treatment with anticoagulants after myocardial infarction and a control group given an ascorbic acid placebo; there were approximately 200 patients in each group. He found the incidence of subsequent infarction to be three times greater in the control group than the treated group; the mortality was eight times more in the control group than the treated group.

Manchester found that the development of angina pectoris subsequent to myocardial infarction was the same in his treated as in his control group. In the anticoagulant group this occurred in 74 (36.2%) and in the control group in 72 (36%). In the anticoagulant group 38 (51.3%) showed improvement as indicated by increased tolerance in walking and performing the Master's two-step test. In the control group 20 (27.5%) showed improvement. In the anticoagulant series there were 4 deaths (5.4%); in the control series there were 30 (41.6%).

Nichol and co-workers [6] have presented a pooled clinical investigation in 1,091 patients with coronary atherosclerosis treated with anticoagulants for 3 to 100 months, for a total of 24,454 months. The average duration of therapy was 22.4 months. Their results were as follows:

In patients without frank infarction (impending infarction), in the treated group of 96 patients there were six deaths, or a mortality of 6.2%; in the abandoned group 32 patients stopped treatment after 315 months and, in a follow-up study over 732 months, the mortality was 18.7%; and in the control group 10 patients were observed for 269 months and there were four deaths, or a mortality of 40%.

In patients who had had one infarction, in the treated group of 735 patients there were 73 deaths, or a mortality of 10%; in the abandoned group 205 patients stopped treatment after 2,423 months and, in a follow-up study over 3,708 months, the mortality was 18.5%; and in the control group 297 patients were observed for 12,376 months and there were 110 deaths, or a mortality of 37%.

In patients who had had multiple infarctions, in the treated group of 260 patients there were 52 deaths, or a mortality of 20%; in the abandoned group 82 patients stopped treatment after 1,246 months and, in a follow-up study over 950 months, the mortality was 56.1% and three were lost to follow-up; and in the control group 110 patients were observed for 3,276 months and there were 42 deaths, or a mortality of 38.1%.

Methods and Material of Present Study

In our clinic, long-term anticoagulant therapy after acute myocardial infarction was initiated 15 years ago. Our study of the accumulated cases has taken well over a year, and no new cases have been included in this study since June, 1956. We interviewed all active patients, obtained hospital records and private physicians' information, and finally contacted patients who had discontinued therapy personally wherever possible. Detailed methods of anticoagulant therapy as used in our clinic have been recently published.[7]

Our report of 521 cases comprises the following groups: (1) long-term anticoagulant therapy for myocardial infarction, 268 patients, and pseudo-

control (discontinued therapy), 140; (2) long-term therapy for coronary insufficiency, 55, and pseudocontrol, 29; and (3) long-term therapy for angina, 23, and pseudocontrol, 6.

We have purposely used the term "pseudocontrol" rather than control in our series of patients who discontinued therapy. The majority of authors have used such patients as controls. This type of control subject, not only in our series but in those of others, has had the beneficial effects of anticoagulant treatment for varying periods before such therapy was stopped. Such beneficial effects from even brief "long-term" therapy are evidenced by lowered mortality figures, as compared to those of completely untreated patients. This will be shown later.

comparing those given anticoagulants for three months to 10 years with those in whom this treatment was discontinued. This group excludes any patient who developed coronary thrombosis. Four (7.3%) of the 55 treated patients died, as compared to 19 (12.9%) of 147 patients not given anticoagulants as recorded in the study of Master and Jaffe. The group recorded in table 4 is not large, but the definite improvement of angina in 27.3% of patients in the treated group with coronary insufficiency and in 30.4% in the treated group with angina without coronary insufficiency is certainly worthy of note.

Hemorrhage.—In the 268 patients on active long-term therapy, the following minor hemorrhagic episodes were noted: purpura (mild), 13; hema-

TABLE 1.—*Comparison of Mortality Estimated for Each Year After Myocardial Infarction**

		Anticoagulant Therapy (Present Study)				Control Group, Mortality (Literature)		Pseudocontrol Group (Present Study)			
				Mortality, %						Mortality, %	
Time Elapsed, Yr.	Infarction†	Cases, No.	Deaths, No.	Yearly	Total	Keyes et al.,‡ %	Av., %	Doing Well, No.	Deaths, No.	Yearly	Total
1	S	213	14	6.2		16.1		109	6	5.5	
	R	39	2	4.9		31.2		24	1	4.2	
2	S	204	8	3.8		27.9		98	12	12.3	
	R	18	3	14.3		39.6		23	0	...	
3	S	173	5	2.8		41.7		82	6	7.3	
	R	10	3	23.1		52.1		19	2	10.5	
4	S	130	6	4.4		41.4		64	5	7.8	
	R	7	2	22.2		62.5		15	1	6.7	
5	S	101	6	5.6	18.3		44.2	52	6	11.5	32.1
	R	6	4	40.0	21.0‡			14	2	14.3	29.3‡
6	S	78	5	6.0				35	2	5.7	
	R	2	0	...				9	3	33.3	
7	S	52	3	5.5				25	1	4.0	
	R	1	0	...				5	1	20.0	
8	S	41	1	2.4				16	1	6.3	
	R	1	0	...				4	1	25.0	
9	S	30	0	...				2	0	...	
	R							1	0	...	
10	S	10	0	...	24.6‡		67.6	1	0	...	35.7‡

* Tabulated in percentage of total patients on anticoagulant therapy for any one year.
† S = Single attack of myocardial infarction prior to anticoagulant therapy; R = recurrent (two or more) attacks before treatment was instituted.
‡ Combined rate for single and recurrent.

Results

In the 268 patients who received long-term anticoagulant therapy after myocardial infarction, there were 62 deaths, or 23.1% of the total series, and 10 recurrent attacks with recovery, or 3.7% of the total series. Of those who died while on anticoagulant therapy, the last-recorded prothrombin time was below 20 seconds in 28 cases. Table 1 summarizes data for this series.

Table 2 summarizes the data in treated patients with classification as to severity, length of time on therapy, and age group. The mortality, by year after therapy was stopped, for patients in the pseudocontrol group is recorded in table 3. It is interesting in this series to note that the mortality is highest in the first few years after discontinuance of therapy. Of the total of 52 who died, 42 patients died within two years after stopping anticoagulant therapy.

In table 4 are listed the results of treatment in patients with acute coronary insufficiency and angina without attacks of coronary insufficiency,

toma, 8; epistaxis, 13 (3 cases of multiple episodes); conjunctival hemorrhage, 5; rectal hemorrhage, 10 (1 case of multiple episodes); hemorrhage from gums, 7 (1 case of multiple episodes); and retinal hemorrhage, 2—a total of 58.

In regard to major hemorrhagic episodes, anticoagulant treatment was temporarily discontinued in two patients who had hematuria and who required hospitalization and blood transfusion. Both are continuing anticoagulant therapy. One episode of rectal bleeding caused the patient to stop this treatment for one year, but it has now been restarted. In patients in whom anticoagulant therapy was permanently discontinued, there were six instances of nonfatal bleeding, including one rather severe case. One patient with slight gastric hemorrhage died three months later of cancer of the stomach.

Recently, unexpected gastric hemorrhage during anticoagulant therapy has, on investigation, revealed an occult visceral malignancy.[8] Hemorrhage has been the main argument against anticoagulant therapy. With the advent of vitamin K_1 preparations,

the possibility of severe hemorrhage is becoming less and less an objection to this therapy. In many instances, a small dose of vitamin K_1 will lower the prothrombin time toward normal within a few hours. It is to be noted, then, that in the entire series there were no deaths due to hemorrhage.

Comment

Interesting statistics on 25-year follow-up studies after myocardial infarction are appearing in the literature. These patients have not been treated with anticoagulant therapy and therefore make a good control group for the present study.

Katz and co-workers,[9] in 1949, reported on 488 patients with myocardial infarction, in some of whom follow-up studies were done for variable periods up to six years. They estimated that about 25% died within the first two months, 50% by the end of the first year, and 75% by the end of the third year.

TABLE 2.—*Age, Length of Therapy, and Severity of Disease in 192 Patients on Long-term Anticoagulant Therapy After Myocardial Infarction*

Length of Therapy, Yr.	Age Group, Yr.						Severity			
	30-39	40-49	50-59	60-69	70-79	80-89	Mild	Moderate	Severe	Recurrent*
1-2	...	3	7	5	3	...	8	7	1	2
2-3	1	8	18	13	2	...	16	18	7	2
3-4	...	5	10	11	1	...	7	7	7	2
4-5	...	3	9	12	1	1	11	10	2	4
5-6	...	1	12	7	2	...	8	9	4	1
6-10	...	6	18	17	7	1	6	30	13	2
10-15	...	...	1	4	1	2	1	2	...	5
Total	1	26	75	69	17	4	57	83	34	18

* Prior to therapy.

In 1951, Sigler [10] reported on a 25-year follow-up study of 1,700 patients with coronary disease. Of the 1,208 patients in Sigler's series who had at least one attack of coronary occlusion, 785 were still alive when this report was compiled. In this series, 45.3% of the males and 37.8% of the females were alive five years or more after the first attack; 10.7% and 10.4%, respectively, were still alive 10 years or more, and 2.1% of the males were still alive 15 years or longer.

Also in 1951, Master and Jaffe [11] reported on survival rates of 412 patients after acute coronary occlusion. They found that 40% made a complete recovery and 25% a satisfactory recovery. Of those who recovered completely, 40% survived over 5 years and 25% survived over 10 years. They reported that the best prognostic guide appears to be the patient's symptoms.

In 1956, Richards and associates,[12] in reporting their own series published following data: Thirty-eight patients died within one month. Forty-nine per cent (79 of 162 patients or 39.5% of the total group) survived 5 years; 31% (50 of 162 patients) 10 years; 14% (23 of 162 patients) 15 years; and 5% (8 of 162 patients) 20 years. Six patients lived more than 25 years after acute infarction.

According to these authors, the best index to long-term prognosis after myocardial infarction is the degree of recovery of the patient after the acute period of infarction. Of the 55 patients in the series of 200 who had "complete" clinical recovery after myocardial infarction, 45 (85%) were alive after 5 years, 31 (56%) after 10 years, and 6 (11%) after 25 years.

TABLE 3.—*Mortality of Pseudocontrol Subjects in Years After Discontinuance of Anticoagulant Therapy**

Time Elapsed, Yr.	Infarction†	Doing Well, No.	Died, No. (Total, 32)	Mortality, %
1	S	70	28	40.0
	R	17	5	29.4
2	S	55	5	9.1
	R	10	4	40.0
3	S	33	3	9.1
	R	7	1	14.3
4	S	23	3	13.0
	R	6	1	16.7
5	S	13	1	7.7
	R	4	0	...
6	S	5	1	20.0
	R	2	0	...
7	S	2	0	...
	R	1	0	...

* Patients had been previously treated with anticoagulants for three months to 10 years.

† S = Single attack of myocardial infarction prior to anticoagulant therapy; R = recurrent (two or more) attacks before treatment was instituted.

These authors also presented the statistics shown in table 5, which include untreated patients with long-term disease in their own group as well as in others' series.

The authors mention that the patients reported in their own series had disease of more than average severity, due to an element of selection by consultation. A considerable number of patients with coronary disease in our series who were given anticoagulants were referred to us by their physicians because of continuing or developing symptoms after the initial attack. It is our belief, then, that in regard to severity of disease our own series, in a general way, is comparable to that of Richards and associates.

TABLE 4.—*Results of Treatment in Patients with Acute Coronary Insufficiency and Angina Without Coronary Insufficiency*

	Acute Coronary Insufficiency				Angina Without Coronary Insufficiency	
	Anti-Coagulant Therapy		Discontinued Therapy		Anti-Coagulant Therapy, No.	Discontinued Therapy, No.
	No.	%	No.	%		
Total cases	55		29		23	6
No angina	48		23		15	4*
Died	4	7.3	3	10.3	0	1
Angina persistent or worse	3	5.5	3	10.3	1	1
Definite improvement in angina	15	27.3	1	3.4	7(30.4%)	0
Recurrences	8	14.5	2	6.9		

* All were improved on anticoagulant therapy before it was withdrawn.

We have briefly reviewed the literature both for statistics on long-term anticoagulant therapy after

myocardial infarction and also for survival rates of patients not given anticoagulant therapy in 25-year follow-up studies now available.

The 10-year mortality of 67.6%, as averaged from the literature, in patients who did not receive anticoagulants would seem entirely disproportional to the mortality of 35.7% in our patients who discontinued anticoagulant therapy after varying intervals. The number of patients (140) in the pseudocontrol group, especially toward the end of their 10-year period, is, admittedly, small. A large series must be reported before such statistics would be comparable. Until such time, certainly no conclusions can be drawn as to possible benefit in later years in those patients who received anticoagulants for varying intervals before discontinuance of this therapy. In all events, mortality in patients on long-term anticoagulant therapy would seem appreciably better than in the pseudocontrol subjects and certainly far superior to those in the completely untreated group. We would feel, then, that in this study of 428 cases our statistics may be of some significance.

TABLE 5.—*Survival Rates in Patients* with Myocardial Infarction*[12]

Author	Cases, No.	5-Yr. Survival, %	10-Yr. Survival, %
Bland, E. F., and White, P. D.: J. A. M. A. **117**:1171-1178 (Oct. 4) 1941	162	49	31
Billings, F. T., Jr., and others: Am. J. Med. **7**:556, 1949	143	45	30
Smith, C.: J. A. M. A. **151**:167-170 (Jan. 17) 1953	85	66	29
Cole, D. R., and others: Circulation **9**:821, 1954	285	67	44
Weiss, M. M.: Am. J. M. Sc. **231**:9, 1956	211	52	37

* Includes only those who lived at least one month after acute infarction.

The question as to selection of cases in which initiation of long-term anticoagulant therapy is indicated has been a subject of discussion. Askey [13] has reflected the opinion of quite a number of observers in stating that continuous long-term therapy is indicated for patients who survive severe or recurrent myocardial infarction or even for those who develop the anginal syndrome not responding to other treatment. In our own series such criteria were followed in many cases. However, for purposes of later comparable statistics certain patients have been placed routinely on such therapy after their first attack.

In the last four years an increasing number of reports has appeared in which statistical studies were given on long-term anticoagulant therapy after coronary thrombosis. In each instance, conclusions drawn were favorable and, at times, enthusiastic. In our own series it is our belief that the statistical evidence would certainly appear favorable and warrants further study. However, we stress the fact that the natural course of coronary disease with all of its variables, including environmental and emotional factors, makes the statistics in this condition difficult to obtain and interpret. Conclusions must be drawn with the greatest caution and objectivity.

Summary

In the present study, there were 268 patients who were given long-term anticoagulant therapy after myocardial infarction and 140 in whom this treatment was discontinued. Eighty-one of the long-term group were treated from 5 to 15 years with anticoagulants. Of these patients, 23.1% died from cardiac disease 1 to 15 years after infarction and 3.7% had recurrences and survived.

In the study of five-year statistics, the mortality in the treated group (combined single and recurrent attacks) was 21.0%, compared with 44.2% in the true control group (as averaged from the literature), in which patients had never received anticoagulant therapy. It is interesting to note in our "pseudocontrol" or discontinued-therapy group that the five-year mortality was 29.3%. Likewise, in a study of 10-year statistics, the mortality in the treated series was 24.6%, compared with 67.6% in the true control group. In the pseudocontrol group the mortality was 35.7% at the 10-year level.

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USE OF NITROFURANTOIN IN CHRONIC AND RECURRENT URINARY TRACT INFECTION IN CHILDREN

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Nitrofurantoin was used in the treatment of chronic or recurrent infection of the urinary tract in 100 children. In each case the diagnosis was confirmed by cystoscopy, urography, and the culturing of a pathogenic organism from the urine. The series included only children who were followed for at least six months and who were able to tolerate the medicament in adequate dosages. The therapeutic dosage was 6 to 10 mg. and the prophylactic dosage 1 to 5 mg. of nitrofurantoin per kilogram of body weight per day. In 36 children all manifestations of infection were stopped by this treatment, without complications or recurrences. In more than half of the patients who showed a good initial response, however, the infection recurred. The recurrence was commonly asymptomatic, being detected by urinalysis and culture. Two case histories illustrate the persistent nature of this infection and the need of continuing prophylactic treatment for at least three months after the urine has become sterile.

During the past four years, nitrofurantoin has been administered therapeutically or prophylactically for periods up to 27 months to 100 children with chronic and recurrent urinary tract infection. All these patients were given follow-up examinations for at least six months. A long period of observation and treatment was found necessary for adequate evaluation and control of this disease. Nitrofurantoin was found to be an effective agent for this disease because of its broad antimicrobial spectrum and its success in controlling most infections initially and other infections by administration for a longer period. Prophylactically, it was successful in suppressing recurrent infection. No serious toxic effects were noted, and there was minimal development of bacterial resistance to this drug.

Recurrent or chronic persistent urinary tract infection is the commonest pediatric urologic problem. Since the symptoms may be minimal, or in some cases entirely absent, the disease is undoubtedly more frequent than generally realized. It is our belief that recurrent infection is not a series of isolated episodes but repetitive exacerbations of one underlying and continuous disease. Because of the frequency with which pathogenic organisms are recovered from urine samples taken directly from the kidney, and because of the high incidence of vesicoureteral reflux in patients with symptoms of cystitis, potential renal infection must be considered even when the syndrome seems to consist only of cystitis. Therefore, we have used the term urinary tract infection, rather than cystitis or pyelonephritis, in discussing the disease in these children.

We feel that, if urinary tract infection is allowed to progress, the atrophic changes of chronic pyelonephritis may eventually develop. The common lay belief that children "grow out of" acute episodes of infection is probably at least partly true, since the incidence of infection in the adolescent period is lower. Nevertheless, we feel that the damage from these prepuberal infections may persist into later life. This is difficult to evaluate accurately. In this series, 96% of the cases of uncomplicated urinary tract infection occurred in girls. During a similar period, of 100 adults seen in consultation for pyelonephritis uncomplicated by other urologic disease or pregnancy, 65% were women. Nine of 14 patients in this group with severe atrophic changes were women. During this four-year period, six autopsies at the Western Pennsylvania Hospital, performed on patients from 20 to 50 years of age, revealed chronic pyelonephritis uncomplicated by other urologic disease as the primary cause of death. This constituted about 1% of the autopsies. Five of the six patients were women.

The time to preserve renal tissue is at the onset of disease. Therefore, we feel it is important to treat these infections promptly and adequately even though the symptoms may be mild or the abnormal findings few other than pyuria and bacteriuria. Nitrofurantoin (Furadantin) has characteristics that make it a valuable drug for long-term administration to control urinary tract infection. These include its lack of toxicity, wide range of antibacterial effectiveness, and reduced tendency to induce development of bacterial resistance to the drug.[1] Our previous studies,[2] indicating that nitrofurantoin is a suitable and effective urinary antimicrobial in children, were confirmed by a study of 52 children in 1956 by Ericsson and co-workers [16] in a Swedish children's hospital. Successful nitrofurantoin treatment of urinary tract infections in children also has been reported by several other clinicians in the

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United States, including Carrol in 1955,[1g] Fetter and Warren in 1956, [1h] Stewart and Rowe in 1956,[1e] and Jawetz and associates in 1957.[1d]

The ability of a drug to sterilize the urine immediately and to produce clinical improvement is not a final criterion of efficacy, since renal parenchymal infection may persist despite sterile urine.[1d] The control of infection can be presumed only after a long period of observation. This study was made and is being continued to determine the effectiveness of nitrofurantoin in controlling these chronic urinary tract infections in children for a prolonged period.

TABLE 1.—*Patients with Urinary Tract Infection and Duration of Treatment*

	Uncomplicated, No.	Complicated, No.
Total	72	28
Boys	3	8
Girls	69	20
Followed >12 mo.	45	21
Received nitrofurantoin for >6 mo.	41	22
Receiving nitrofurantoin at time of evaluation	24	14

Materials and Methods

One hundred infants and children with chronic or recurrent urinary tract infection were treated with nitrofurantoin for variable periods up to 27 months (table 1). The therapeutic dosage was 6 to 10 mg. and the prophylactic dosage 1 to 5 mg. of nitrofurantoin per kilogram of body weight daily. The diagnosis was based on clinical history and examination, including cystoscopy, urography, urinalysis, and a urine culture demonstrating a pathogenic organism. A severe anatomic abnormality of the urinary tract or neurogenic bladder disease was present in the 28 patients classified as having complicated urinary tract infection. Those children who had follow-up periods of less than six months, who received inadequate medication due to intolerance, or on whom concurrent surgery was performed are not included in this report. Patients who voided from a rectal reservoir or who had a foreign body in the urinary tract were not included because no more than transient sterilization of the urine was accomplished in such cases. Among the 72 patients with uncomplicated urinary tract infection, there were many with minor abnormalities, such as vesicoureteral reflux, reduced urethral caliber, or cystitis cystica.

The follow-up studies lasting 6 to 48 months included clinical observation, urinalysis, urine culture, and further urologic study when indicated. Periodic blood examinations were carried out. Of the 100 patients, 66 had follow-up studies of over one year, 10 of these of over three years. No case was considered controlled unless the urine was sterile and the centrifuged urinary sediment microscopically normal. We feel that the method we used to evaluate urine cultures was satisfactory clinically. A growth of pyogenic bacteria on a two-drop plate was considered significant. Pyogenic organisms present only in a broth culture were considered significant when they were the same as those recovered during acute clinical infection. In the absence of pyuria, using the study of Clabaugh and Rhoads,[3] we disregarded the organisms of low pathogenicity commonly present in the urethra.

In some children, urinalysis showed normal findings but the culture persistently showed pathogenic organisms. If treatment was discontinued in these children an exacerbation of clinical infection often occurred. Therefore, we have considered a culture of a pyogenic organism to be significant in all but a few isolated instances, and, in the final determination of those cases considered controlled, no culture contained pyogenic bacteria.

Results

Nitrofurantoin was successful in controlling the urinary tract infection in 82% of these 100 children (table 2). In the group without complications it was 92% successful. Recurrences were either eliminated or reduced in incidence, duration, and severity. By readministering or increasing the dosage of nitrofurantoin the infection was controlled again in all but six patients. In three of these, control was obtained by another antimicrobial. While the results were not as satisfactory in patients with a marked anatomic abnormality, we believe it significant that the infection was controlled in 57% of these patients. In two patients infection was controlled prior to pyeloplasty, facilitating postoperative recovery. Other patients, whose infections could not be classified as controlled, had variable degrees of clinical improvement.

Nitrofurantoin was administered for long periods to patients whose infections were resistant to all other antimicrobials, and this drug eventually controlled these infections in seven children (table 3). Seven patients whose infection is not now controlled are currently receiving nitrofurantoin therapy of 3 to 13 months' duration.

This study confirmed our opinion that urinary tract infection is a persistent disease, since infection recurred in more than half of the patients who showed a good initial response (table 2). This frequency of recurrence increases with the length of follow-up period. In a considerable number of these children the recurrence was asymptomatic and discovered only by urinalysis and culture. Unfortunately, it is difficult to get some parents to bring their children back for these visits when the latter

TABLE 2.—*Results of Nitrofurantoin Treatment in Chronic Urinary Tract Infection*

	Uncomplicated, No.	Complicated, No.
Controlled		
No recurrence	36	8
Recurrence with prophylactic dosage, recontrolled by therapeutic dosage	6	5
Recurrence when nitrofurantoin was discontinued, recontrolled by readministration	24	3
Recurrence when nitrofurantoin was discontinued, recontrolled by administration of another antimicrobial	3	0
Not controlled	3	12

are asymptomatic or have few symptoms. Therefore, the true incidence of recurrence is undoubtedly higher than we have reported.

Nitrofurantoin has been effectively administered prophylactically for as long as 27 months, with infrequent development of drug-resistant bacteria. This was demonstrated, first, by the successful retreatment with nitrofurantoin of recurrent infection in 27 children and, second, by successful control of recurrent infection in children taking a small prophylactic dosage, by increasing the dosage to a therapeutic level. Nineteen of the 24 patients in the group with uncomplicated infection and 8 of the 14 patients with complicated disease are currently taking nitrofurantoin because of recurrent infection after the drug was withdrawn. The infections are controlled at this time apparently because nitrofurantoin treatment is being continued. Therefore, in about one-quarter of the entire reported series of patients, more or less continuous nitrofurantoin therapy has been required to control infection. It was our observation that, while 1 to 2 mg. per kilogram of body weight per day was effective in preventing recurrence of infection in most patients, some of them required a daily dosage of two to three times that amount.

The broad antibacterial spectrum of nitrofurantoin is important because of the variety of organisms encountered initially (table 4). Frequently, a different organism may be encountered either during the course of treatment or when infection recurs after treatment is discontinued. This change of organism during the course of observation occurred in 39 of our patients. A total of 210 organisms was encountered initially, during recurrence of infection, or when the organism changed during treatment in these 100 patients (table 5). The tabulated results are not synonymous with a clinical control of infection, since in some cases when an organism was

TABLE 3.—*Summary of Infections Successfully Controlled Only by Long-term Nitrofurantoin Therapy*

Case No.	Complication	Original Organism	Time Required for Control, Mo.
1	Neurogenic bladder	Esch. coli	13
2	Neurogenic bladder	Ps. aeruginosa	10
3	Neurogenic bladder	Ps. aeruginosa	11
4	None	Proteus	5
5	Cystitis cystica	Ps. aeruginosa	5
6	Cystitis cystica; vesicoureteral reflux	Proteus	6
7	Cystitis cystica; previous nephroureterectomy for hydronephrosis	Esch. coli	3
8	Previous nephrectomy for renal vein thrombosis	Proteus	6
9	None	Ps. aeruginosa	6

eliminated it was simultaneously replaced by another. They do indicate that nitrofurantoin is effective against a wide range of organisms.

No serious toxic effects were encountered in any patient in this series. Two patients noted patchy alopecia, and nitrofurantoin was withdrawn. On recurrence of a urinary tract infection clinically resistant to all other antimicrobials, nitrofurantoin was readministered and the alopecia did not recur. One patient who became drowsy on two occasions while taking nitrofurantoin was not treated with it again. In several patients, a mild rash appeared during treatment but the drug was not withdrawn and the rash disappeared. There was one Negro

TABLE 4.—*Bacteriological Findings in Patients with Urinary Tract Infection*

	Uncomplicated, No.	Complicated, No.
Initial organism		
Esch. coli	32	10
Proteus	28	16
A. aerogenes	4	0
Paracolobactrum species	3	1
Ps. aeruginosa	3	3
Gram-positive cocci	9	2
Mixed infection	7	4
Change in organism during treatment or when infection recurred	24	15

patient, but no alteration in the blood findings of any patient was observed. Variable degrees of gastrointestinal intolerance, manifested by anorexia, nausea, and vomiting, were seen. The incidence of intolerance is difficult to determine, since whether it is tolerated may depend on the persistence of the parent in administering the medicament. When the parents are convinced of the necessity of administration the incidence of complete intolerance is low, although the daily dosage may have to be reduced. The newer flavored suspension is better tolerated. Those who refuse the suspension may accept a tablet crushed over a spoonful of syrup or honey or mixed with a carbonated beverage, peanut butter, or fruit preserves.

Report of Cases

Three case reports, representative of the various problems encountered, are presented. The first shows the control of recurrent infection of the urinary tract for a two-year period by vigorous and prolonged nitrofurantoin therapy.

CASE 10.—A 3-year-old girl was first seen on Sept. 23, 1953, with a history of recurrent abdominal pain, frequency, dysuria, and pyuria. The condition could be temporarily relieved by antimicrobials. She was acutely febrile at that time and was receiving sulfisoxazole (Gantrisin) and penicillin. Physical examination was normal except for a temperature of 103 F (39.4 C). Cystoscopic examination showed nothing abnormal, except for a urethral stricture which was dilated. The upper urinary tract was normal. Urinalysis revealed pyuria. Escherichia coli and hemolytic streptococci were obtained on culture of the urine. Nitrofurantoin was given for a four-day period, but one month later pyuria was still present although the patient was asymptomatic. Nitrofurantoin therapy, 10 mg. per kilogram of body weight daily, was administered for a week and continued at half that dose for the next two months. Cultures during therapy and at its conclusion were sterile. During 1954, the patient had no urinary symptoms and six urinalyses and cultures showed no recurrence of infection. On May 31, 1955, occasional enuresis was noted. A urinalysis demonstrated pyuria, and a culture again showed Esch. coli. Nitrofurantoin was again prescribed, first 8 mg. and later 4 mg. per kilogram of body weight daily for a total of 10 weeks. Urinalyses and cultures during and at the conclusion of therapy showed no further infection. During the remainder of 1955 and 1956 and up to March 14, 1957, urinalyses showed normal findings and the cultures were sterile.

The next case illustrates infection controlled only by continuous prophylactic nitrofurantoin therapy. Infection recurred during prophylactic administration, which necessitated an increase in the dosage for control.

Case 11.—This 8-year-old girl was first seen on Sept. 10, 1953, with a history of intermittent fever, frequency, and pyuria for five years. Treatment with various antimicrobials produced only transient relief. Urinalysis demonstrated pyuria, and urine culture showed a growth of Esch. coli. An anatomically normal urinary tract was seen on cystoscopy and pyelography. Nitrofurantoin, 8 mg. per kilogram of body weight daily, was given for two weeks. Urinalyses and cultures showed normal findings until Jan. 11, 1954, when pyuria recurred and a urine culture again grew Esch. coli. Nitrofurantoin, 8 mg. per kilogram of body weight per day, was given with a good result and the dosage was gradually reduced to 2 mg. per kilogram of body weight daily, but on Aug. 6, 1954, pyuria and bacilluria with Esch. coli recurred. An increase in dosage to the original amount controlled the infection by Aug. 30, 1954, and the dosage was reduced to 4 mg. per kilogram of body weight per day. On this dosage the infection did not recur, and nitrofurantoin therapy was discontinued on March 24, 1955. She did not return until Dec. 31, 1956. She was asymptomatic, but a few pus cells were found on urinalysis, together with a marked bacilluria with Esch. coli. Nitrofurantoin, 9 mg. per kilogram of body weight daily, cleared the urine, and a dosage of 3 mg. per kilogram has maintained a sterile urine. On July 20, 1957, cystoscopy and pyelography again demonstrated a normal urinary tract. There was no vesicoureteral reflux, and excretion of intravenously given phenolsulfonphthalein at that time was 65% in 30 minutes.

Table 5.—*Effect of Nitrofurantoin on 210 Organisms*

Type of Organism	Times Encountered, No.	Eliminated by Nitrofurantoin, %	Eliminated by Other Antimicrobial, %	Not Eliminated, %
Esch. coli	110	88	3	9
Proteus	68	72	9	19
Ps. aeruginosa	19	68	5	27
Cocci	13	84	8	8

In case 2 (table 3), control of resistant infection was achieved by prolonged therapeutic treatment with nitrofurantoin despite the presence of a neurogenic bladder, due to meningomyelocele, and resistant organism. Recurrence was prevented for a period of one year by prophylactic treatment with nitrofurantoin.

Case 2.—A 5-year-old girl was first seen on Sept. 23, 1955, because of incontinence. She had a meningomyelocele repaired during a previous hospitalization, but there was a residual sacral neurological inadequacy. No effort had been made to control urination, and she was constantly wet. Residual urine was 50 cc., and the capacity of the bladder was 120 cc. Cystoscopy showed evidence of chronic cystitis, trabeculation, and cellule formation. The upper urinary tract appeared normal except for slight left ureterectasis. Urine cultures grew Proteus organisms. On urinalysis, the specific gravity was 1.018; the reactions for sugar and albumin were negative, but the centrifuged urinary sediment contained many pus cells. The child was made to empty her bladder by suprapubic pressure every two hours, and with this routine she remained dry during the day. Nitrofurantoin, 7 mg. per kilogram of body weight daily, was prescribed, but after three months pyuria was still present and the urine culture demonstrated Pseudomonas aeruginosa. During the next six months this organism was consistently present. A course of polymyxin therapy did not eliminate the Ps. aeruginosa, and nitrofurantoin therapy was continued. On June 19, 1956, urinalysis gave normal results and the urine culture showed no growth. The dosage of nitrofurantoin was gradually reduced to 2 mg. per kilogram of body weight per day, and subsequent urinalyses showed no pyuria and urine culture gave negative findings. There has been no change in symptomatology, with an uninfected urine.

Conclusions

Chronic or recurrent urinary tract infection in children is a persistent disease, inherently resistant to treatment. Follow-up studies must be done for long periods of time, with frequent urinalyses and urine cultures. Nitrofurantoin is an effective and nontoxic drug which is suitable for both therapeutic and prophylactic use. There is apparently little risk of development of drug-resistant bacterial mutants. Chronic urinary tract infections should be treated with a daily therapeutic dosage of 7 to 10 mg. of nitrofurantoin per kilogram of body weight given for at least two weeks after the urine has become sterile and the urinary sediment microscopically normal. A prophylactic dosage of 2 to 4 mg. per kilogram of body weight per day is then given for at least three more months. If this dosage is not tolerated it may be reduced, but a longer period of treatment can then be anticipated. If infection recurs after nitrofurantoin has been withdrawn, the same schedule should be repeated but prophylactic treatment continued for a longer period of time. Any nonremediable abnormality of the urinary tract necessitates prolongation of treatment, depending on its severity. Nitrofurantoin therapy should not replace surgical treatment when such is indicated.

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FRACTURES OF THE TIBIAL PLATEAUS

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In cases of fracture of the tibial plateau the question whether to use open or closed methods of treatment must be answered by considering all the factors that may determine the degree of permanent residual disability. Since continued use of a deformed knee is likely to cause late arthritic changes, deformity that cannot otherwise be corrected is the primary indication for surgical procedures. In a series of 63 fractures of this kind, open reduction was considered necessary in only 7. The closed, nonoperative treatment used in the other 56 cases included these features: aspiration of free blood and joint fluid, manipulation with the patient under general anesthesia to correct deformity, skeletal traction, early motion, transfer from splint to brace, protection during the period of healing, and a program of exercises begun early and continued over a period of months. Unprotected weight-bearing cannot be permitted until union is solid (about six months), and a certain amount of permanent residual disability may be expected.

The great majority of fractures of the tibial plateaus can be treated successfully by nonoperative means. Only a small percentage of these common injuries are best handled by open reduction.[1] The question as to which fractures are best handled by operative and which by nonoperative means is one that often tries the best surgical judgment.

These injuries are often complicated, and no matter how they are handled a certain amount of permanent residual disability may be expected. There is always a long period of severe temporary disability during their healing, since unprotected weight-bearing cannot be permitted until union is solid. In the cancellous bone of the upper tibia this is not complete for about six months.

Residual Disability

The degree of permanent disability is influenced by roughness of joint surface, presence of deformity, associated injuries to structures within and/or outside the joint, avascular necrosis, epiphysial arrest, muscle atrophy, and contractures. The greater the degree of roughness and articular irregularity produced by the fracture, the earlier and more severe will be the degenerative changes within the joint. Probably a more important factor in the late development of traumatic arthritis is the presence of valgus, varus, or back-knee deformity. Since most of these fractures involve the lateral tibial plateau, valgus deformity is more common than either of the other two.

The degree of injury to the articular cartilage, to the meniscus, and to other structures within the joint is often unsuspected prior to operation. This fact has led certain authors [2] to make especially strong statements as to the need for open reduction in the great majority of tibial plateau fractures.

Injuries to soft tissue structures outside the joint also have an adverse effect on residual disability. Fractures of the tibial plateau have been called "the bumper fracture" because the mechanism of injury not infrequently is that of an automobile bumper striking the lateral aspect of the knee. The bruising effect of such a blow often predisposes to thrombophlebitis, and it may actually contuse or tear the peroneal nerve; both of these complications add to residual disability.

Avascular necrosis of the detached comminuted fragments is most apt to occur after operative intervention. The blood supply to these fragments is interfered with, not only by the fracturing and displacing force but also by the surgeon as he lifts them out to try to fit them together into a normal relationship.

Epiphysial arrest can occur only in the child. It is just as apt to occur in the epiphysial fracture with little displacement as in those with marked displacement. The muscle atrophy of disuse increases the disability. Muscle action is said to be the first line of defense of a joint; the ligaments are only secondary means of maintaining joint integrity.

Fibrous adhesions have been shown to form within the joint, extending from the raw bone of the fractured plateau to the patella and to the infrapatellar fat pad.[3] Unless motion is begun early and continued, these adhesions become dense fibrous bands which effectively prevent motion. Actual contracture of the fibrous tissue capsule or of the fibrous tissue within the muscles, tendons, and ligamentous structures will occur when these fractures are treated by prolonged immobilization. In the young patient, stretching of these contractures about the knee is usually only a matter of normal use, but in the elderly person the contractures may lead to permanent disability. It is to be noted that a

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majority of these injuries occur in people above the age of 50. In this series, only 12 out of 63 were younger than that age.

The decision as to whether to use open or closed methods in the treatment of any individual case is based on a consideration of the factors influencing the degree of permanent residual disability. When confronted with a specific patient, the surgeon will ask himself which factors he hopes to eliminate by doing open surgery and which factors can be altered as favorably or more favorably by closed rather than open methods. It is questionable, for instance, whether the surgeon will be able to make a more smooth and regular joint surface than would have resulted had operation not been done. Early

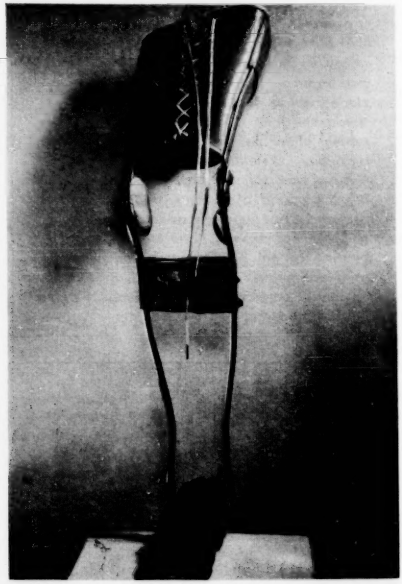

Fig. 1.—Long-leg, double-bar brace with free ankle motion, lock-knee, and adjustable pressure pads.

motion of the uninjured femoral condyle on the multiple small fragments of the tibial plateau tends to mold them into position. At operation the surgeon often finds that he must excise the lateral meniscus whether it is torn or not in order to obtain adequate exposure of the plateau fragments. He then finds that the cancellous bone has been crushed and that there is no longer enough bone substance to permit the jigsaw fragments to be put together perfectly. Some sort of bone graft usually must be used in order to support the fragments, and the result is, at best, an approximation of smoothness. One may ask if the irregularity of the joint surface really is so important in the production of permanent residual disability. The defect left in the articular surface of the knee when a large osteochondritis dissecans fragment is removed commonly causes little or no appreciable arthritic change, even after many years. The same is true with the defect left after the removal of an osteocartilagenous fracture fragment. These defects in the articular surface fill in with scar tissue, and, with weight-bearing, a metaplasia occurs and fibrocartilage is formed. While not perfect, this repair appears to be serviceable as far as knee function is concerned.

Associated injury to the structures within or without the joint either do not require surgical treatment or can be done as secondary procedures at a later date. Avascular necrosis is more, not less, apt to occur with surgical intervention. Epiphysial arrest is not affected one way or the other by surgery, and muscle atrophy and fibrous tissue contractures are the result of immobilization and disuse. This leaves, then, the one factor of deformity as the major consideration in the decision to do an open reduction. If the fracture is such that the best position that can be obtained by a closed method will still result in an appreciable valgus, varus, or back-knee deformity, then open reduction is indicated. This group is a relatively small one—in our series of 63, open reduction was carried out in only 7, approximately 11%.

Nonoperative Treatment

An outline of the nonsurgical treatment of tibial plateau fractures is as follows: (1) aspiration, (2) manipulation to correct deformity, (3) skeletal traction, (4) early motion, (5) brace, (6) protection during period of healing, and (7) exercises. The patient is admitted to the hospital. The distended joint is aspirated of the free blood and joint fluid. Aspiration serves two purposes: it makes the patient much more comfortable and it facilitates physical diagnosis, since one can then more readily visualize and palpate the anatomic landmarks. Skeletal traction is then applied by means of a Kirschner wire through the os calcis or through the lower end of the tibia, and the leg is placed in a Thomas splint with a Pearson attachment. The manipulative reduction of the fracture, with the patient under general anesthesia, need not be considered an emergency. The patient is comfortable in bed in traction, and the manipulation may be done at the convenience of the surgeon and after the patient has had proper preoperative preparation and medication.

Active and active-assistive motion with the leg in traction in the Thomas splint is begun the next day. The splint is applied in such a way that by pulling a rope placed conveniently at hand the patient himself assists in moving the knee through a range

of motion from complete extension to flexion of 70 to 90 degrees. At first the patient will require encouragement to permit and to perform such extension, but as the days go by it becomes easier for him to obtain the full range of motion permitted by the splint.

When this has been accomplished, a transfer from the splint to a brace may be made. This is a double-bar long-leg brace with free ankle motion, lock-knee, and adjustable medial pressure pad (fig. 1). The medial pressure pad is used to prevent any tendency toward the development of a valgus deformity and to force weight-bearing on the medial plateau only if the patient accidentally places his weight on the injured leg prior to its healing or when graduated weight-bearing is begun. At first he will wear the brace all of the time, removing it only with help for skin care. Later, the brace may be left off at night and for underwater exercises. Weight-lifting exercises to increase quadriceps power are begun very early with the brace on and must be continued over a period of months. Ambulation with brace and crutches may be permitted early, depending on the coordination and general status of the patient.

Fractures of the tibial plateaus include epiphysial fractures; "T" or "Y" fractures; fractures of the medial tibial plateaus; and fractures of the lateral tibial plateaus. Epiphysial fractures seldom represent any problem in residual disability, except those which result in early closure of the epiphysis. This is just as apt to occur in fractures with minimal as in those with major displacement. The fracture line often passes partly through or along the epiphysial plate and partly through the bone, so that closure is apt to occur on one side, giving a valgus or varus deformity. Muscle atrophy, stiffness, and contractures seldom give trouble in children. Reduction of the fracture by manipulation with the patient under general anesthesia is usually not difficult, and the fracture is stable and the position readily maintained in a long sleeve cast. Only occasionally will a hip-spica cast be required. Weight-bearing with crutches may be begun in four to six weeks and nonprotected weight-bearing in three to four months.

Nearly all "T" and "Y" fractures can be handled by the nonoperative method described above. Open reduction, with or without internal fixation, need be used only in those cases in which there is wide displacement of fragments or downward displacement of one plateau only which cannot be reduced by manipulation and which, if permitted to remain, will result in a varus or valgus deformity.

Report of Cases

Case 1.—A 74-year-old man with marked diabetes fell from a stepladder in April, 1954, and sustained depressed fracture of the posterior half of the lateral plateau (fig. 2). Traction was used for three weeks and then a brace and crutches. He was discharged from the hospital one month after the injury. One year later, he stated that he had regained full function with ability to go up and down stairs normally and to carry on his usual activities without discomfort. I estimated that he had approximately 15% permanent partial disability because of 15 degrees of flexion deformity with further flexion possible to 80 degrees. He had a valgus deformity of 10 degrees on the involved side as compared with 5 degrees on the opposite side.

Case 2.—A 27-year-old man fell and injured his knee in November, 1953. He had minimal displacement (fig. 3A). The cast was bivalved after two weeks, and motion was started. Six weeks after the injury, he slipped and fell on elevated stairs while walking with crutches in a half-shell cast, reinjuring his knee (fig. 3B). Manipulation was done with the patient under general anesthesia. A brace was applied and early motion started. He was last seen in November, 1956 (fig. 1C), when he stated that he had very little trouble with his knee. He had continued in his work and had recently completed a 16-mile hike. He had complete extension and flexion to 80 degrees. There was slight valgus deformity, some instability, no pain, good muscle tone, and slight atrophy.

Case 3.—A 57-year-old man was in an automobile accident in March, 1956, when he sustained a minimal fracture of the lateral tibial plateau. A cast was applied, and

Fig. 2 (case 1).—Fracture of posterior third of lateral tibial plateau; no instability with knee in extension.

he was permitted to be up on crutches. He developed thrombophlebitis while on a business trip to the West Coast. The cast was removed and treatment of the thrombophlebitis instituted. He was transferred to Evanston Hospital seven weeks after the original injury. He had been walking on the unprotected leg. X-ray at this time showed considerable depression of the plateau (fig. 4). He was fitted with a brace, and exercises were begun. He was last seen in January, 1957, when he stated that he was symptom-free, played golf, was not restricted in his activities, and had normal range of motion, no instability, and good muscle power. He was heard from but not examined in January, 1958, when he was still symptom-free.

Fractures of the medial tibial plateau are rare in comparison with the lateral tibial plateau fractures and are handled in exactly the same way. All of those fractures which involve a small fragment only, where there is slight displacement of less than a quarter of an inch, or which involve the posterior

third or half of the plateau only and some of the fractures with depression of central fragments, with or without separation of the peripheral rim, have been treated by nonoperative methods. Surgical replacement of fragments was restricted to those cases in which the development of a valgus deformity could not otherwise be prevented.

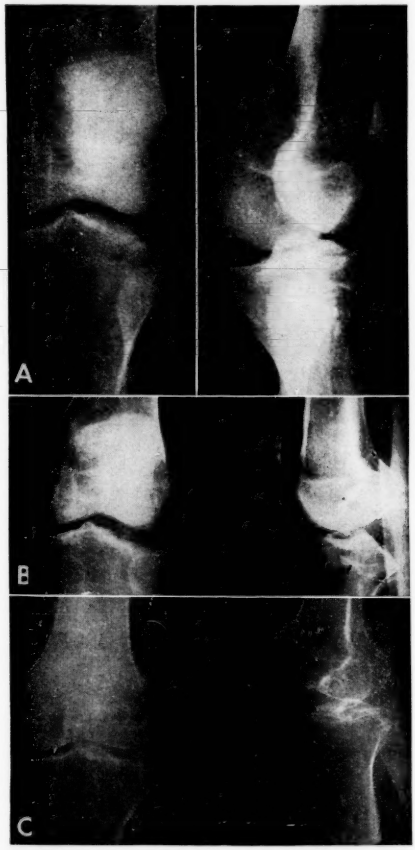

Fig. 3 (case 2).—X-rays showing, *A*, minimal displacement after fracture in November, 1953, *B*, marked crushing and comminution after second fall on Jan. 14, 1954, and, *C*, condition three years later.

Summary

Most fractures of the tibial plateaus result in some degree of permanent residual disability, whether operative or nonoperative treatment is used. Continued use of the knee in valgus, varus, or back-knee deformity is probably the greatest factor in production of late arthritic changes. Deformity which cannot otherwise be corrected is the primary indication for surgical procedures. A method of conservative, nonoperative treatment is based on aspiration, manipulation, and reduction with the patient under general anesthesia, skeletal traction, and early motion and exercise.

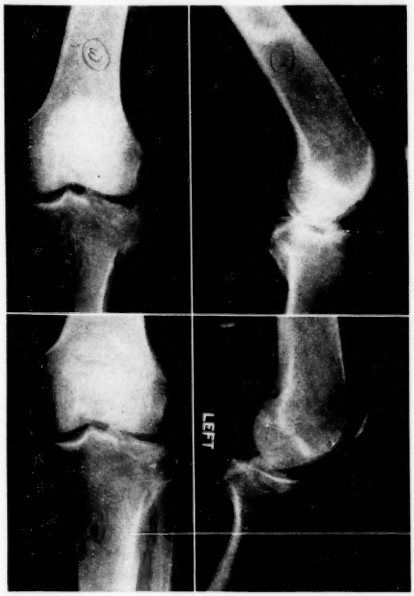

Fig. 4. (case 3).—X-rays taken 10 weeks after original undisplaced fracture of lateral tibial plateau. Patient had walked with no protection for his knee, without permission.

636 Church St.

The case reports included in this study were taken from the records of the orthopedic service of the Evanston Hospital, with permission.

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BRINE BATH TREATMENTS FOR DECUBITUS ULCERS

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The brine bath is part of an active program of treatment for decubitus ulcers. The brine is a solution of 5% crude rock salt and 2.5% magnesium sulfate. The temperature is about 37.8 C (100 F) at the beginning but should be adjusted to the patient's tolerance; it is allowed to decline during the 20 minutes of administration. The Hubbard tank is preferred to a tub because the patient can be more easily helped and underwater exercise can be given. The bath is part of the local treatment, which also includes other forms of physical therapy and may call for surgery; in addition the general condition of the patient needs attention. Motivation and instruction in self-care may be necessary. These recommendations are based on experience with some 1,400 patients with spinal cord injuries over a period of 12 years, with an average of 20 patients receiving brine baths each day.

Patients with spinal cord injuries are prone to develop decubitus ulcers. These are one of the most frequent complications and are due to two factors: (*a*) neurogenic disturbances of metabolism in the involved tissues and (*b*) pressure at a bony prominence. When the patient is in the supine position pressure is directly applied against the heels, sacrum, posterior iliac region of the spine, and scapulas. When the patient is in the prone position pressure is directly applied upon the knees, anterior iliac region of the spine, and on the elbows when the upper part of the body is supported upon them. When the patient is in the side position pressure is applied directly to the lateral aspects of the distal and proximal ends of the fibula and to the areas of the greater trochanter of the femur. When he is in the sitting position in bed with the head end of the mattress raised to a 45-degree angle, a shearing force is applied over the sacral area,[1] and when he is in the sitting position in a wheel chair pressure is applied directly to the areas of the ischiatic tuberosities. If the ischiatic tuberosities have been surgically removed because of decubitus ulcers, pressure, in the sitting position, causes an ulcer in the area between the ischiatic tuberosity and the greater trochanter, described by Comarr [2] as the intertrochanteric area, and sometimes in the perineal area.

Pressure on the lateral and medial malleoli of the ankles from braces and tension of the soft tissues over the lateral malleolus from contractures causing inversion of the foot at the ankle must be prevented, either by conservative measures or by surgery. Pressure sores on the medial aspects of the knees due to excessive spasticity in the adductors of the thighs usually demand surgical correction by means of obturator neurectomy and adductor myotomy bilaterally. At the onset of the decubitus ulcer, the skin is only reddened, and, as has been described previously,[3] blanching of the reddened skin by finger pressure indicates the absence of thrombosis in the underlying vessels and the reversibility of the local skin condition. This is achieved by relief of pressure, frequent turning, sponge rubber doughnuts, air foam mattresses, and other indicated measures.

Inflammation of the skin and phlegmon may extend to ulceration under the following conditions: (*a*) prolonged pressure that has occurred over the reddened area; (*b*) skin that has not been kept dry but has been moist from excessive sweating or from additional moisture collecting under dressings, bedclothes, or clothing; (*c*) general physical condition impaired due to infection of the genitourinary system, upper respiratory infections, gastrointestinal disturbances, nutritional deficits, or anemia; or (*d*) a disturbance of homeostasis that occurred owing to some unknown cause. Various initial skin lesions are observed—abrasions, cellulitides sometimes resembling erysipelas, bursitis, or local soft tissue gangrene—and any one of these conditions may eventuate in osteitis or osteomyelitis. Depression may accompany the physical deterioration and may even precede it, necessitating a program which includes improving the morale and motivation of the patient.

Patients with spinal cord injury are prone to develop an anemia. When a decubitus ulcer occurs the hemoglobin values range frequently from 10 to 12 Gm. per 100 cc. and not uncommonly are from 6 to 8 Gm. per 100 cc. in patients with multiple decubitus ulcers. The hematocrit value is also low. The total serum protein level is low, and the albumin-globulin ratio tends to be reversed. The blood urea nitrogen level may be high if renal damage is present. The low hemoglobin level results in poorer tissue oxygenation for purposes of tissue repair, inadequate protein levels additionally contribute to poor nutrition of the tissues, and both deficits result in weakness, decreased circulation, and stasis. Proteins are lost through the exudative fluids of the ulcer, and nitrogen balance in severe cases may be

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difficult to maintain. Proteins may also be lost through the kidneys at one time or another, and protein losses during necessitated bed rest in the presence of decubitus ulcers are increased.[4] The absorption of necrotic substances from decubitus ulcers over prolonged periods may result in amyloidosis.[5]

Carcinoma can occur in an ulcer, and suspicion of such is an indication for surgery. One of 1,354 patients with spinal cord injuries [6] at the Veterans Administration Hospital, Long Beach, Calif., was a veteran of World War I in whom a sacral ulcer had been present from 1940 to 1948. He developed a tumor which was successfully removed, and the ulcer was repaired. The patient is 66 years of age and is still doing well at the time of writing.

As stated previously, deep ulcers tend to invade the periosteum and bone, and an osteomyelitic process starts in an osteoporotic bone. Lowman and Roen [7] reported favorable treatment for osteomyelitis by means of brine baths in a salt pool as early as 1924. Because Lowman's results in osteomyelitis and pyarthrosis were impressive, brine bath treatments for decubitus ulcers were started at the Veterans Administration Hospital in 1946. From 1946 to 1950 this treatment was used primarily for preoperative preparation. Once the ulcers were filled with granulating tissue and free from necrosis, surgical repair was done. Since 1950, the brine bath technique has been improved and now a majority of ulcers heal without surgical repair.[8] In ischial and trochanteric decubitus ulcers, recurring bursas usually necessitate surgical removal. Brine baths hasten and supplement general and local treatments and are the best means to provide a clean surgical field. There have been some 1,400 patients with spinal cord injuries in the past 12 years, and among them the number treated daily by brine baths has averaged about 20. Brine bath treatments are only one part of the over-all treatment, and each part of the over-all treatment demands meticulous attention in order that best results be achieved. The average duration of the use of the brine bath treatment for a gangrenous ulcer is about three months.

The attention given to the bacteriological flora from 1946 to 1950 was found to be of relatively minor importance, and it is known that a mixed infection existed. The recommended brine solution is bacteriocidal, yet not injurious to tissue cells. Too high a concentration is contraindicated because it is detrimental to tissue cells. On the other hand a decrease of concentration leads to a reduction or loss of bacteriocidal quality. A brine solution of 5% crude rock salt and 2.5% magnesium sulfate has been found to be most effective.

General Treatment

The general treatment of the patient consists of maintaining nutritional balance, correcting anemia and hypoproteinemia, prevention of prolonged pressure by frequent turning, anabolic hormone therapy, and general hygiene. In addition, attention should be paid to proper hydration, to controlling urinary infection, and last but not least to psychological support.

Diet.—The diet must be high in protein. It should contain a variety of animal, vegetable, cereal, and yeast proteins so that the amino acids essential to tissue anabolism are present in the blood. The foods which are rich in proteins are meat, liver, fish, fowl, eggs, beans, peas, milk, whole wheat bread, and whole wheat cereals. Protein hydrolysates are not well tolerated but may cause anorexia and interference with the ingestion of the regular meals and thus may actually decrease the protein intake. The above-mentioned foods are high in iron content except for the milk which is arbitrarily limited to a glass with each meal because of a possible danger of calculosis. Second helpings with each meal and multiple feedings are to be encouraged. A high amount of vitamins should be contained in the diet. Fruits and vegetables help in supplying this need. If nausea and vomiting are present, a dextrose-vitamin preparation (Trinidex), 1,000 cc. given intravenously, is administered daily, in addition to other intravenously given fluids. When intravenous injections are no longer necessary, the diet can be supplemented with multivitamin tablets, such as thiamine or vitamin B complex, as indicated.

Restoration of Normal Hemoglobin Level, Red Blood Cell Count, and Hematocrit Values.—The restoration of the hemoglobin level to normal is best achieved by transfusions of 500 cc. of blood once, twice, or three times a week, as indicated. It is generally considered that 15 Gm. of hemoglobin per 100 cc. of blood is the normal level, and it is amazing how much faster the ulcers heal when accidentally the hemoglobin level may reach 16 or 17 Gm. However, because of other factors, it is advisable to keep the hemoglobin at a level of 14.5 to 15.5 Gm. Liver is rich in iron and is beneficial when served at least once a week. When needed, 1 cc. of crude liver extract with 2 mcg. of vitamin B_{12} is given intramuscularly every other day. Iron medicaments are given orally when the hemoglobin level has returned to nearly normal, and, although the effect is slower than with the transfusions, 5 grains of ferrous sulfate, three times daily, and other iron medicaments are usually well tolerated for moderately long periods. The results from iron medicaments are too slowly obtained for the acute early treatment. If in the presence of low serum proteins, severe edema and anasarca occur, the administration of normal human serum albumin, 50 cc. (12.5 Gm.) once or twice a day, is indicated.

Frequent Turning of the Patient.—The patient should be turned every two hours, and if sacral or trochanteric ulcers are present a Foster bed or Stryker frame is used. The turning of the Foster bed or Stryker frame should so be timed as to allow

feeding in the supine position, which should be achieved 30 minutes before meals. If only one decubitus ulcer is present a regular hospital bed may be used, care being taken that the patient never lies on the ulcer.

Hormone Injections.—In cases of anorexia and slow healing in spite of all other supportive treatments, testosterone injections of 25 or 50 mg. daily for from two to four weeks are used for their anabolic effect. A second course of this therapy may be given after a rest period of two to four weeks.

General Hygiene.—Contact sweating below the level of the lesion is present in patients with spinal cord injury and with complete lesions due to direct stimulation of the sweat glands. In addition, in patients with complete lesions, excessive sweating below the level of the lesion can occur from irritation coursing along the neurones of the rootlets and roots of the distal cord segment. Dressings may be necessary at one time or another, but as soon as the ulcer is granulating and free from slough, it should be exposed to air without dressing and protected by a bed cradle.

The patient is given a daily cleansing bath with warm water and soap as a normal skin hygiene. Alcohol rubs and talcum powder have been generally dispensed with but are occasionally used for comfort when indicated.

Bowel movements should be regulated every other day. Oral intake of psyllium hydrophilic mucilloid (Metamucil), mineral oil, and occasionally milk of magnesia, and rectal application of glycerin suppositories may be used supportively.

Exercises for the normal muscles of the upper extremities, neck and trunk, deep breathing exercises, and standing on a tilt table or standing at a standing bar are started early. These exercises improve respiration, circulation, muscle tone, and metabolism. Deconditioning or disuse atrophy is also thereby diminished or prevented.[8]

Restoration of Adequate Fluid Intake and Urinary Output.—If a patient with deep ulcers is dehydrated, it is necessary to start the daily intravenous administration of fluids with 2,000 cc. of 5% glucose solution in distilled water, 1,000 cc. of 5% glucose solution in isotonic sodium chloride, and 1,000 cc. of dextrose-vitamin preparation, until the fever subsides. As soon as the oral fluid intake becomes adequate, the intravenous administration of fluids is discontinued. An adequate oral intake is usually provided by a glass of water at hourly intervals from 7 a. m. to 7 p. m., in addition to the fluids taken with meals.

If the function of the bladder is well balanced in regard to capacity and residual, no further therapy is indicated. If imbalance, vesicoureteral reflux, or pyelonephritis are present, dependent intraurethral catheter drainage is instituted during the emergency period, and, as soon as the need is passed, the reflex emptying of the bladder should be reestablished, according to Bors.[9]

Antibiotics and Other General Medicaments.—In patients with high fever, antibiotics are usually used—most frequently, a form of penicillin (Crysticillin), 300,000 units, and streptomycin, 0.5 Gm., twice daily. If these do not suffice, a tetracycline, 500 mg., in 1,000 cc. of 5% solution of glucose in distilled water is given daily, intravenously, slowly. When the need for intravenous administration is past, this can be followed up with orally given tetracycline, 250 mg., four times daily. When the urinary infection no longer requires the use of antibiotics, sulfisoxazole (Gantrisin), 0.5 Gm. four times daily, may be given orally.

Motivation.—Patients who are admitted with large decubitus ulcers have usually undergone a period of inadequate care in regard to general hygiene, diet, local treatments, and genitourinary system. Concomitantly there is a mental depression. The morale and motivation improve gradually with good medical and nursing care, proper diet, good general hygiene, and attention to personal appearance, such as shaving and brushing the teeth. Bowel care, exercise, bathing, proper local ulcer care, adequate genitourinary care, and psychotherapy are also essential.

Summary.—The general treatment of the patient includes consideration of diet (proteins, calories, and vitamins); correction of anemia and hypoproteinemia (with transfusions, iron therapy, and normal human serum albumin); prevention of prolonged pressure (with Foster bed and Stryker frame); anabolic hormone therapy; general hygiene; proper hydration (intake and output); antibiotics and general medicaments; and motivation.

Local Treatment of Decubitus Ulcers

Débridement.—The local treatment of the decubitus ulcer is just as important as the general treatment of the patient. Baruch [10] described the valuable effect of whirlpool or hydromassage therapy in the cleansing and healing of wounds and the promotion of the separation of dead tissue as early as 1920. Occasionally, where a large necrosis is present, careful débridement is indicated. Small eschars, if kept dry, heal without interference on removal of pressure. If infection occurs underneath the eschar, it should then be débrided.

Elimination of Direct Pressure.—The elimination of direct pressure on all ulcers is the most important factor in local treatment.

Brine Bath.—The cleansing and healing process of a gangrenous ulcer is augmented by the use of a brine bath from three to five times a week (fig. 1 and 2). The brine solution which has been used most satisfactorily at this hospital is a solution

containing 5% crude rock salt and 2.5% magnesium sulfate. This concentration provides a favorable osmotic effect and is at the same time bacteriocidal.

A Hubbard tank is preferred to a tub for tetraplegic patients because of easier access. Such a bath will require about 100 gal. of water and approximately 40 lb. of crude rock salt and 20 lb. of epsom salt. A 6-ft. tub will require about 50 gal. of water, 20 lb. of crude rock salt, and 10 lb. of epsom salt. An arm or leg bath tank may require 25 gal. of water, and a foot bath tank may require about 15 gal. The percentage of brine solution remains the same.

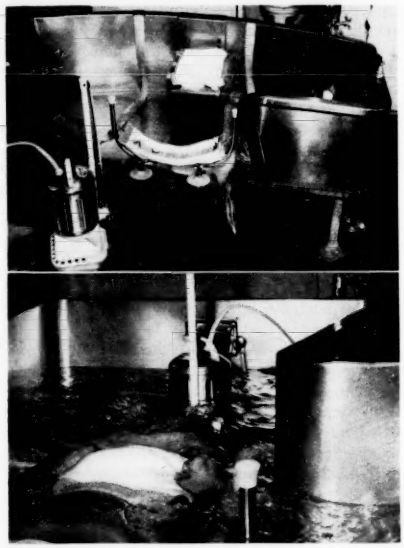

Fig. 1.—*Above*, equipment for Hubbard tank brine bath, showing head rest and axillary support straps for tetraplegic patients. Body support in center has canvas sling adjustable to different heights. Jacuzzi whirlpool unit is in foreground. This stainless steel Hubbard tank has been in use for over 12 years, and corrosion from brine is minimal. *Below*, tetraplegic patient receiving brine bath treatment in Hubbard tank for sacral ulcer. Jacuzzi whirlpool unit is between lower extremities. Temperature of brine solution is checked with mercury thermometer.

In the Hubbard tank and in the tub, underwater exercise can be used passively, actively, and with assistance as indicated. Because of the osteoporosis of the bones, skill, experience, and judgment must be applied in regard to passive and assistive motion. The general increase in body temperature from the warm brine solution aids the general metabolism and circulation. The force of gravity on the limbs is diminished by the floating effect of the brine solution, muscle tension is reduced, pain and spasticity are reduced, and as a result active motion in weak muscles is enhanced. In addition, the pressure of the water upon the skin and upon the abdomen helps to improve the circulation by tending to collapse the superficial veins of the skin and by compressing the abdominal viscera, thus changing the dynamics in the vascular system.[7] Therefore, the depth of the bath is important.

Chlorinated tap water which flows through a mixing valve at a starting temperature of 100 F (37.8 C) is used. This temperature is usually well tolerated even by patients with complete cervical spinal cord lesions and who are poikilothermic, but caution should be used in determining the patient's tolerance to heat. The bath temperature declines about 4 to 8 degrees during its 20-minute duration. This temperature is comfortable and remedial in that it provides a mild vasodilation.

Whirlpool action improves the circulation of the blood and the flow of the lymph. The Jacuzzi whirlpool is used at a distance of 12 in. from the ulcer, with a flow of 45 gal. per minute. The flow is directed up the limbs and over the ulcer. The flow can be easily adjusted from 45 gal. per minute down to zero. The distance of the machine from the ulcer can be increased as desired. The flow can be either direct or indirect against the wall of the tub or tank. The flow can also be used directly on the feet for about five minutes to improve the mobility of the soft tissues through gentle massage. This massaging effect is more gentle and beneficial than manual massage. However, when the tissue surrounding the ulcer is heavily scarred and adherent to the underlying bone, deep circular manual friction massage may be necessary to loosen the soft tissues from the bone. Figures 3, 4, 5, and 6 show results of the brine bath treatment.

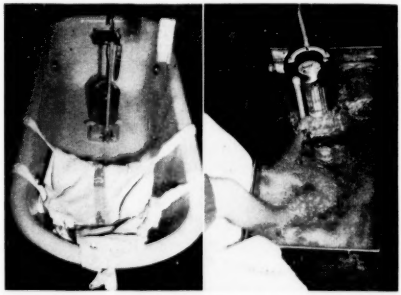

Fig. 2.—*Left*, equipment arrangement in former continuous-flow 6-ft. tub. Canvas sling supports upper part of body, permitting good flow of brine solution under and around buttocks, hips, and sacral areas. *Right*, brine foot-bath whirlpool treatment being given for decubitus ulcer of heel. This part of treatment in latter stages can be followed up at home.

Ultraviolet Radiation.—When the patient is removed from the bath, a suberythemal dose of cold quartz ultraviolet radiation with the Birtcher hand

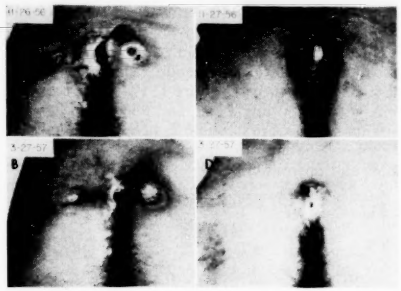

Fig. 3.—*A*, sacral ulcer on which surgical closure had been attempted and, *B*, complete healing at former tension suture buttonholes and remaining small sacral ulcer ready for buried grafts. *C*, sacral ulcer in paraplegic patient and, *D*, ulcer almost completely healed. (After 31 treatments ulcer was ready for buried grafts on 1/25/57.)

unit is applied to the base of the ulcer at a distance of 1 in., starting with 15 to 20 seconds of application and increasing the time 1 to 2 seconds each treatment up to a maximum of three to five minutes. Both the brine bath and ultraviolet radiation stim-

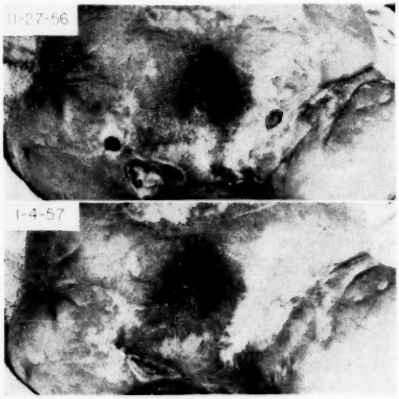

Fig. 4.—*Above*, multiple recurrent ulcers of buttocks in paraplegic patient with bilateral thigh amputations. *Below*, ulcer on right, healed after 23 treatments, and remaining ulcers ready for surgical closure.

ulate the growth of granulation tissue and possess bacteriocidal action.

Local Treatment on the Ward.—If a deep ulcer crater exists, it is filled with granulated sugar, on the patient's return to the ward. Its action is hygroscopic and cleanses the ulcer by osmosis. More sugar may be added two or three times a day if necessary. Occasionally, a solution of 10% Peruvian balsam in a cod-liver oil ointment base is applied to the ulcer to promote healing. If a greenish-colored discharge denotes the presence of a pyocyaneous growth, boric acid powder, 2% solution, or 10% boric acid ointment may overcome this in a few days.

A superficial ulcer filled with clean granulation tissue is exposed to air and sunshine. The beneficial use of a bed cradle has been mentioned above. A protective dressing with cod-liver oil ointment can be used when the patient starts ambulating in a wheel chair.

In the early stages, when the general condition of the patient does not permit the use of a brine bath,

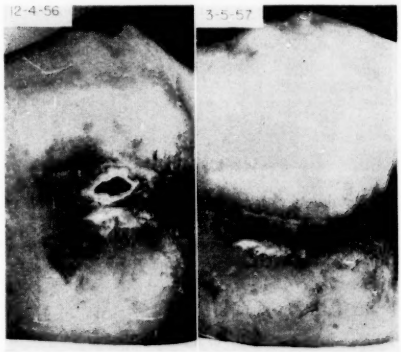

Fig. 5.—*Left*, sacral ulcer and discoloration with swelling of greater trochanter in patient with cervical spinal cord injury. *Right*, completely healed sacral area and improved condition at right trochanter.

a Dakin's pack is used locally. Dakinization by irrigating tubes is also useful in cases of deep bursas and small sinus opening.

If a cellulitis is present, elevation of the extremity and local wet packs with use of Domeboro's solution or Domeboro's solution with equal parts of 70% alcohol are beneficial. Domeboro's solution is made up with one tablet (2½ grains) in 100 cc. of distilled water, forming a solution of aluminum sulfate and calcium acetate. The U. S. P. solution is 1:10, or Burow's solution.

A bursa beneath an ulcer is usually infected and is aspirated, or incised and drained, and will require definitive operative correction. Operation will also be indicated if a sequestrum remains. If the granulation tissue becomes excessive it is burned off level with skin surface with a silver nitrate stick. A temporary measure for thin epithelialization of a sacral ulcer filled with clean granulation tissue is by means of small buried grafts of split-thickness epithelium.[11]

When a small sinus persists, healing has been obtained by following up the above treatments with short-wave diathermy, 150 ma., for 15 minutes, with 1 to 2 in. of toweling between the drum and skin surface, staying within tolerance of the tissues to heat at all times. Microwave treatments have been used beneficially on penoscrotal fistulas, with use of director C at 2 in. for 20 minutes at 20% power, in addition to brine baths, giving five treatments weekly. If operative closure is performed, ulcer excision with bursectomy and ostectomy is the method of choice. For any patient who tends to

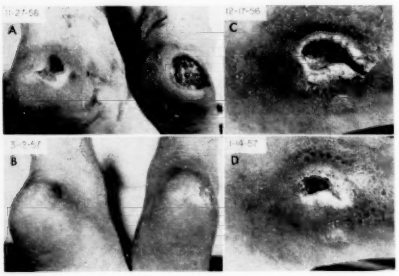

Fig. 6.—A, burns on heels of paraplegic patient from self-administered hot water bottle and, *B*, excellent epithelialization two and one-half months later. *C*, ulcer, recurrent for three years and now present for several months, over lateral aspect of external malleolus of left ankle and, *D*, ulcer after 10 brine foot-bath treatments ready for excision with partial resection of distal end of fibula.

develop decubitus ulcers, it must be stressed that an ounce of prevention is worth more than a pound of cure, and when healing has been obtained, the patient must be instructed to avoid pressure.

Summary.—Local treatment of the decubitus ulcer consists of débridement; elimination of direct pressure; brine bath (with controlled temperature, chlorination, 5% crude rock salt and 2½% epsom salt [for osmotic action, bacteriocidal action, and stimulation of granulation tissue], Jacuzzi whirlpool action, and proper duration and frequency of treatment and depth of brine bath); ultraviolet radiation (with emphasis on time and distance of dosage, type of lamp, stimulation of granulation tissue, and bacteriocidal action); and local treatment on the ward (with sugar, Peruvian balsam, boric acid, exposure to air and sunshine, Dakin's solution, Domeboro's solution, silver nitrate stick, shortwave diathermy, microwave, surgical indications, and prevention).

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HEALTH GUIDANCE IN PREADOLESCENCE.—There is a greater interest in adolescence than ever before. In fact some people believe that just as the period of infancy and early childhood formerly received a concentration of attention in pediatrics and public health, so we are now moving toward the adolescent and devoting more time to his problems of growing up and seeking independence in our ever more complex society. In adolescence psychologic problems take on greater significance. As teen-agers are apt to look elsewhere than to their own parents for guidance, the schools through counselors and others often have an opportunity to be helpful to them. Many parents are unprepared to cope with the various phases of adolescent development. For many years health workers have emphasized anticipatory guidance for parents of preschool children, but only recently has it been suggested that similar guidance might be offered to parents of pre-adolescent children. . . . Problems of adolescence may well be the major challenge of our generation, just as infant mortality was for the previous one.—A. J. Lesser, M.D., Changing Emphases in School Health Programs, *Children*, January-February, 1958.

GRANULAR URETHRITIS IN WOMEN

SURVEY OF THREE HUNDRED PATIENTS TREATED BY CYSTOSCOPIC FULGURATION

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Granular urethritis is a chronic infection that smolders in the urethra for months or years and causes a variety of misleading nonurinary symptoms. Backache, the most frequent of these, was present in 261 (87%) of 300 patients and was located most often in the sacral region with or without radiation into the thighs. Pus was absent from urine specimens obtained by catheter unless infection also existed in the bladder or upper urinary tract. The treatment by fulguration here described was carried out in the hospital with the patient under anesthesia induced by thiopental sodium. Correct postoperative care is essential, and the patient should be observed for at least three months. In a series of 300 women so treated 263 returned for final evaluation three or four months after fulguration, and all except 35 reported complete relief of their urinary symptoms. Among 185 who were followed for longer periods, more than half had no recurrences.

Granular urethritis is a common pathological entity in women which is frequently overlooked and undertreated in the general practice of medicine. It is a chronic infection that smolders in the urethra for months or years with periodic episodes of acute symptoms that too often are labeled "cystitis" and treated solely by oral medication.

Certain characteristics of this condition may be highly misleading to those practitioners not fully aware of the diagnostic and therapeutic pitfalls. Pyuria is characteristically absent in the catheterized specimen unless, of course, there is an associated cystitis or upper urinary tract infection. The nonurinary complaints may overshadow the urinary symptoms. A constant sacral ache may be attributed wrongly to arthritis or chronic back strain, suprapubic discomfort to the uterus, lower quadrant pain to the ovary or appendix, and dyspareunia to some gynecologic cause. Because so many of these women become nervous and easily fatigued there is an inclination to consider them psychoneurotic. Under the influence of antibacterial drugs the urinary symptoms frequently will subside only to reappear weeks or months later.

When chronic urethritis reaches the stage where granulations are numerous, I have seen no treatment but fulguration effect a cure. During my earlier years of urologic practice I relied mainly on urethral dilatations and instillations, and it was gratifying to note that the majority of the women so treated obtained symptomatic relief, although the granulation in the urethra persisted. This accounts for the relatively small number of cases reported in the five-to-eight-year postoperative period. Disillusionment resulted when these patients returned periodically with recurrence of their symptoms. Observation has convinced me that vaginitis and cervicitis play an important role in the etiology and pathogenesis of urethritis, and substantiating data will be presented.

Report of Cases

This series is composed of 300 private patients who had granular urethritis uncomplicated by such conditions as Hunner's ulcer, vesical neck contracture, or neurogenic bladder. The age groups were as follows: 7 patients, 11-19 years of age; 58, 20-29; 90, 30-39; 61, 40-49; 55, 50-59; 26, 60-69; and 3, 70-75.

From the Department of Urology, Rugeley and Blasingame Clinic and Hospital.

The postoperative interval varied as follows: from 4 to 11 months, 58 patients; one year, 129; two years, 47; three years, 32; four years, 20; five years, 7; six years, 3; and seven-eight years, 4. The urinary symptoms in order of frequency were diurnal frequency, 201 patients; discomfort on urination, 123; nocturia, 105; urgency, 90; feeling of incomplete emptying, 57; slow stream or straining, 39; constant desire to void, 29; constant urethral discomfort, 3; and enuresis, 2. Diurnal frequency was often more pronounced in the morning. The women with a feeling of incomplete emptying had no residual urine and had the desire to void again a short time after bladder evacuation. The large majority of those patients who complained of a slow stream had a normal urethral caliber, which indicates that granulations, villi, and polypoid masses may interfere with free urinary flow.

Table 1 summarizes the nonurinary symptoms. Backache occurred most frequently (87%) and was located most often in the sacral region with or without radiation into the thighs. Twenty-seven patients had pain in the flank area and the costovertebral angle, 19 of whom had normal pyelograms. Of the remaining eight, there was marked

renal ptosis without hydronephrosis in three, ptosis with mild hydronephrosis in two, and reduplication of the pelves and ureters in three. All were relieved by fulguration except one who had ptosis with mild hydronephrosis and who obtained a good result after nephropexy and ureterolysis. The results of 65 upper urinary tract studies were as follows: normal, 45 patients; right ptosis (no hydronephrosis), 9; right ptosis (mild hydronephrosis), 5; reduplication of pelves and ureters, 5; and mild ureteropelvic junction obstruction, 1.

Seventy-one per cent of the patients complained of discomfort or pain in the lower abdomen, frequently accompanied by mild abdominal distention. Many patients described a feeling of fulness, aching, pressure, pelvic heaviness, or a sensation as though they were about to menstruate. Dyspareunia occurred in 22% and was readily accounted for by a tender urethra which rebelled at any pressure along the anterior vaginal wall. The aver-

TABLE 1.—*Summary of Nonurinary Symptoms*

Symptoms	No.
Backache	261
Sacral	126
Hips (bilateral)	92
Hip (right)	15
Hip (left)	7
Costovertebral angle and flank (right)	17
Costovertebral angle and flank (left)	10
Lumbar (bilateral)	9
Coccygeal	5
Abdominal discomfort	213
Suprapubic	156
Lower abdomen (right)	22
Lower abdomen (left)	13
Groin (bilateral)	11
Groin (right)	7
Groin (left)	4
Dyspareunia	67
Lower extremity discomfort	62
Thighs	55
Calves	8
Fever	31

age woman rarely volunteered this complaint, and it was usually elicited by direct questioning. The site of lower extremity discomfort, present in 20% of the patients, was most often the thighs, especially on the posterior aspect and frequently as an extension of sacral ache. Eight (2.6%) had cramping in the calf muscles, particularly at night. Low-grade fever occurred in 10% and had been present for weeks or months. Fatigue and nervousness was common, although no exact statistics are available.

Examination

Cystoscopy was done routinely with the McCarthy panendoscope, because superior visualization of the urethra is obtained through its Foroblique lens, affording a view of areas that otherwise would be missed by the right angle lens. The bladder and its trigone were carefully inspected and the bladder capacity determined. Male sounds were gently passed to determine the caliber of the urethra and the external urethral meatus. The anterior vaginal wall was palpated to detect the presence of tenderness, induration, or mass. Bimanual pelvic examination was done and the vagina and cervix were carefully examined. If there was evidence of vaginitis or abnormal discharge, the appropriate laboratory tests were done to determine the cause. If the cervix appeared diseased, consultation was obtained with the gynecologist.

The cystoscopic findings were as follows: 139 patients had normal bladders; 137 had chronic trigonitis; 32, mild trigonitis; 79, moderate trigonitis; 26, severe trigonitis; and 24, acute cystitis. All 300 patients had granulation of the urethra; 51 had polyps; 55, meatus stricture; 24, urethral narrowing; and 7, caruncle. Note that at the time of the initial examination 46% of the patients had normal bladder and trigone.

The urine was pus-free in all except the 24 women with cystitis and a few with severe trigonitis. Granulation tissue was most prominent in the proximal one-third to two-thirds of the urethra, and involved the anterior, posterior, and lateral walls. Numerous villi and polypoid masses were commonly associated and probably represented an advanced stage of the inflammatory process. Stricture of the external urethral meatus was found in 18%, the majority of which varied from 16 to 23 F. Urethral narrowing was observed in 8%, and varied from 18 to 25 F.

Vaginitis was found in 72 patients (24%) at the time of the initial examination. There were four types: menopausal, 25; monilia, 21; nonspecific, 15; and trichomonas, 11. Chronic cervicitis was present in 38 (13%), and cystocele in 35 (12%).

Treatment

All forms of vaginitis were cured before proceeding with the fulguration. The gynecologist cauterized the cervix when indicated; this was done in 24 patients before and in 14 at the time of the fulguration. All women with cystoceles who had residual urine or stress incontinence were advised to have reparative surgery. Ten of these repairs were done concomitantly with the urethral fulguration. If the bladder capacity was reduced, gravity irrigations were used to improve it. If the urethra readily accommodated sounds to 27 F. and the bladder and trigone were normal, the patient was given sulfisoxazole (Gantrisin) tablets for one week prior to fulguration. If urethral resistance was encountered, weekly dilatations were performed until sounds to 28 F. could easily be passed. Meatotomies were done with patients under local anesthesia when indicated. If there was an associated cystitis or severe trigonitis, sulfisoxazole was given for two weeks and cystoscopy repeated. The anatomy of the female perineum was carefully explained to each patient with use of illustrations and simple sketches. Emphasis was placed on the

proper use of toilet tissue after urination and defecation, as well as the correct method of douching as advocated by Biskind.[1]

All fulgurations were done in the hospital with patients under thiopental (Pentothal) sodium anesthesia. Intravenous urograms were previously ordered when indicated. The urethra was first dilated to 32 F., and meatotomy was done if the urethral meatus offered resistance or became blanched during passage of the sounds. A Bugbee electrode was used through the 20 F. sheath of the panendoscope, activated by the Wappler surgical unit set at 30. All granulations and polyps were thoroughly fulgurated with use of short bursts of current while the panendoscope was moved in the direction of the bladder. As the bladder became more distended with water, the walls of the more distal portions of the urethra separated to a greater degree, facilitating the procedure in this region. Urethral caruncles were completely excised. The patient was returned to her room without a catheter, except when cystocele repair was also performed, and she was ordinarily dismissed the next morning and allowed to resume her usual duties. Coitus was advised against for at least four weeks and carbonated and alcoholic drinks and highly seasoned foods were prohibited for three months. Four tablets daily of sulfisoxazole with 50 mg. of phenylazodiamino-pyridine hydrochloride (Azo Gantrisin) were prescribed for two weeks.

The first follow-up visit occurred five weeks after dismissal, at which time 1 oz. of nitrofurazone (Furacin) solution was instilled into the bladder and sounds to 27 F. were passed. If urethral resistance was encountered, additional dilatations were performed at weekly intervals; otherwise the patient was next seen two months later for cystoscopic examination. If the urethra easily admitted a 29 F. sound and the trigone appeared normal, the patient was discharged; otherwise additional visits were scheduled. The essential facts of perineal care were reviewed, and the patient was advised to seek prompt treatment of any abnormal vaginal discharge. Those who had an asymptomatic cystocele were told what symptoms to expect, such as stress incontinence, should this condition become more pronounced in the future.

Complications.—Complications were few and of mild degree. In the early postoperative period there was either no dysuria or, at most, minimal burning on urination. Between the second and third weeks mild to moderate discomfort was not uncommon, but, by the end of five weeks, most patients voided with comfort. Intermittent terminal hematuria occasionally appeared during the early weeks, but only two patients had episodes of total gross hematuria. One cleared spontaneously and the other stopped promptly after catheter drainage for 24 hours. Five women had acute retention while in the hospital but voided freely after removal of the Foley catheter the next morning. No patients developed incontinence or urinary fistulas. There were no urethral strictures or bladder neck contractures as a result of the fulguration, but 26 patients noted some slowing of the urinary stream between the first and the third months. This symptom disappeared after several additional dilatations.

Results.—Three to four months after fulguration 263 patients returned for final evaluation and all except 35 reported complete relief of their urinary symptoms. Seventeen became asymptomatic after further treatment: Two underwent cystocele repair, one had correction of marked uterine retroversion, two were treated for monilial vaginitis, three for menopausal vaginitis, two for nonspecific vaginitis, and seven complained of slowness of the urinary stream which was relieved by additional urethral dilatations. Fifteen continued to have nocturia one to three times, two had diurnal frequency, and one had mild urgency. Among this group two had cystocele and three had anxiety neuroses. Thus a total of 18 (6%) were improved but continued to have mild urinary symptoms. Lower abdominal symptoms had disappeared in all but 10 patients, of whom 2 had diverticulitis of the colon, 3 had spastic colitis, 2 had endometriosis, 1 had a periumbilical hernia, 1 had a marked cystocele which was later successfully repaired, and 1 had uterine congestion with tender uterosacral ligaments. In all but seven backache was relieved. Three had severe osteoarthritis, one had a chronic infection of the cervix which was relieved by cauterization, and in three the cause was not clear but chronic back strain was suspected. Those women with dyspareunia had established normal conjugal relationships by the end of three months. Two patients obtained complete comfort only after the gynecologist had corrected uterine retroversion with a pessary. In none had fever persisted. Endoscopic examination revealed absence of the previous urethral infection; the mucous membrane appeared smooth and healthy looking, and previous urethral tenderness had disappeared. In those patients with an associated vaginitis the urethra exhibited various degrees of inflammation which subsequently subsided.

TABLE 2.—*Appearance of Trigone After Treatment in 111 Patients with Trigonitis*

Degree of Previous Infection	No.
Normal trigone	84
Mild	29
Moderate	45
Severe	10
Improved appearance	24
Mild	0
Moderate	12
Severe	12
Not improved	3
Mild	0
Moderate	0
Severe	3

Table 2 compares the appearance of the trigone in 111 patients who had previously had various degrees of trigonitis.

Follow-up Studies

Letters were sent to all of the 300 patients requesting information as to their status since their final visit. Replies were received from 185, or 62%, and have been divided into groups based on the number of recurrences of symptoms. Group 1 consists of 101 patients (54%) who reported no recurrence of their previous symptoms. The post-fulguration intervals are as follows: 23 patients, 6-11 months; 54, one year; 10, two years; 9, three years; 3, four years; and 2, five-six years. Fifteen of these women returned for a routine examination up to five years later, and no recurrence of granulation was observed.

In group 2 were placed the 48 patients (26%) who had one brief mild recurrence of urinary symptoms. Also included are those patients who later developed symptoms from their cystocele, such as nocturia and stress incontinence. The post-fulguration intervals were: 4 patients, 6-12 months; 18 patients, one year; 7, two years; 10, three years; 5, four years; 3, five years; and 1, seven years. Of these patients, 42 returned for reexamination shortly after recurrence of symptoms. It was found that 11 had monilial vaginitis; 10, menopausal vaginitis; 10, cystocele; 7, cervicitis; 2, nonspecific vaginitis; and 2, no gynecologic disease. One had nervous diuresis and the other had symptoms related to her period. Five of the seven with cervicitis required cauterization of the cervix. In the 10 patients with cystocele the findings were otherwise normal; 5 were relieved after repair while the remaining 5 have not as yet consented to surgery. In 30 the urethral mucosa was inflamed, but there was no recurrence of granulation. None has had any trouble since correction of the associated gynecologic disease.

Group 3 includes 26 women (15%) who have had two recurrences of urinary symptoms or who have had one episode of acute cystitis. Their post-fulguration intervals were as follows: 11 patients, one year; 6 patients, two years; 3, three years; 5, four years; and 1, five years. Seventeen of the 26 returned for examination at which it was found that 6 had menopausal vaginitis; 4 had trichomonas vaginitis; 4, nonspecific vaginitis; 2, monilial vaginitis; 2, cervicitis; 4, cystocele; 1 was pregnant; and 1, post partum. In seven women acute cystitis was present, while the remainder had varying degrees of urethritis.

Group 4 consists of 10 patients (5%) who have had more than two recurrences of urinary symptoms or who have had more than one episode of acute cystitis. The post-fulguration intervals were as follows: one patient, one year; five, two years; two, three years; and two, five-six years. Only five women returned for reexamination. Two had menopausal vaginitis and have had no further trouble since this has been treated. In two no gynecologic disease was found, and in one there was some degree of urethral narrowing.

Comment

In addition to various urinary symptoms, the majority of these women had discomfort in the regions of the back, hips, legs, and lower abdomen, which Powell [2] explains as due to lymphatic stasis in the floor of the pelvis secondary to the inflammatory process in the urethra. This results in spasm of the pelvic muscles, particularly the piriformis, which originates between the first to fourth anterior sacral foramens and may cause referred pain in the areas supplied by the sacral plexus. This muscle passes from the pelvis through the greater sciatic foramen and may, when spastic, compress the sciatic and posterior femoral cutaneous nerves as they pass between it and the superior gemellus muscle. Occasionally the common peroneal nerve will branch prematurely from the posterior tibial nerve and actually pierce the piriformis. The superior and inferior gemelli, the obturator internus, and the piriformis all take origin from within the pelvis, attach to the greater trochanter of the femur, and can readily account for pain in the hip regions. Levator ani and coccygeal muscle spasm may cause discomfort in the pelvic and coccygeal areas. Powell [2] reports a hastening of symptomatic relief by digital massage of the piriformis muscle. There were 25 patients with no renal disease who had pain in the renal area, probably as a result of lumbar muscle spasm. It is interesting that six of these, or 24%, had a strictured external urethral meatus.

The fact that the nonurinary symptoms may simulate other conditions is illustrated in the cases of four women in this series who had surgical procedures which failed to relieve their lower abdominal discomfort. One patient, aged 41, had her uterus, ovaries, and ovarian tubes removed and a subsequent appendectomy; another, aged 32, two years previously had had her right ovarian tube and ovary removed; another, aged 36, continued to suffer for eight years after a hysterectomy; while another, aged 33, had had her uterus removed six months before. Many of the so-called psychoneurotic patients became less tense, slept better, and had more energy. The duration of symptoms varied from a few months to many years. One patient, aged 42, wrote that for the past 4 years she has enjoyed more comfort than she had had for the previous 20; another, aged 60, reported that she has been free of symptoms for the past year after having had trouble for 20 years. A low-grade fever occurred in 10% of this series; therefore, chronic urethritis should be considered in any differential diagnosis of unexplained mild fever. Strictures of

the external urethral meatus were common and were seen in 55 women, all of whom underwent meatotomy. Twenty-four had some degree of urethral narrowing, so that in a total of 79 women (26%) there was an obstructive factor.

Associated gynecologic disease was frequent, and I have been fortunate in having the services of a gynecologist readily available in a clinic group. The vaginal secretions constantly bathe the external meatus and are frequently a focus of infection; the intimacy of the lymphatic drainage of the cervix and lower urinary tract is well known. Fifty-one patients (17%) had to have cauterization of the cervix; in 24 it was done before, in 14 at the time of, and in 13 after fulguration. Gross pus was often obtained from the deep glands of the cervix during this procedure. Cervicitis and various forms of vaginitis were associated with most of the recurrences of urinary symptoms in the follow-up period. The treatment of menopausal vaginitis is recommended because of the secondary lowering of resistance to infection in the vagina and urethra. The condition responded to daily instillations of estrogenic cream for at least four weeks, along with the oral intake of small doses of estrogen. The additional use of Furestrol urethral suppositories (nitrofurazone 0.2%, diperodon hydrochloride 2%, and diethylstilbestrol 0.0077% in water-dispersible base) would appear to have been effective, although this preparation was of too recent origin to have been given an adequate trial in this series. It is important that the patient be made aware of the possibility of future recurrences of this condition.

There was no increase in morbidity among the 24 patients who underwent urethral fulguration and cervical cauterization or cystocele repair at the same time. Chronic trigonitis disappeared or improved in the great majority of patients in whom it was present at the time of the initial examination, which would indicate that it is an extension of the infection in the posterior urethra. It is significant that, although urethral dilatations alone are beneficial, 10 patients in this series had had an adequate number of such treatments elsewhere with little or no improvement. Also, some women tolerate repeated dilatations poorly and soon discontinue their visits when faced with a protracted period of this type of therapy.

It is essential that all women who have had urethral fulguration be followed over at least a three-month period, and none should be dismissed until the urethra easily admits a 29 F. sound. Each patient should thoroughly understand the proper hygiene of the perineal area.

Summary

This report analyzes a series of 300 women with granular urethritis who were treated by cystoscopic fulguration of the urethra. The pathological changes were the result of chronic low-grade infection, best demonstrated by employing the Foroblique lens on cystoscopic examination. The patients ranged in age from 11 to 75 years. Pyuria was absent in those patients who did not have an associated cystitis. The nonurinary symptoms, of which backache (87%) and lower abdominal discomfort (71%) were most common, may simulate other pathological conditions. Drugs and urethral dilatations, while helpful, were not curative. Vaginitis was seen in 24% and chronic cervicitis in 12% at the time of the initial examination. Recurrences of the urinary symptoms in the follow-up period were most often associated with gynecologic disease. A follow-up period of six months to seven years was possible in 185 patients in this series, of whom 54% had had no recurrences, while 26% had had one mild episode of urinary symptoms.

105 Hawes St.

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CANCER OF THE LUNG.—Smoking is a complex social phenomenon which in the mid-twentieth century has grown to such proportions as to constitute a threat to the public health quite beyond our past expectancy. It is a formidable problem, though other and more recalcitrant if less widespread forms of drug addiction have been successfully tackled and overcome. Merely to sound the alarm may stimulate some to a successful effort to abandon smoking, but with many it only increases their anxiety and to these we should try to offer more practical help. There is no simple remedy, but explanation, education, group discussion, hypnosis, simple relaxation techniques and alternative forms of mouth satisfaction such as sucking, chewing or biting are helpful, and along with any other possibility which appears promising, ought to be energetically tested and explored. Cancer of the lung should now be regarded as largely preventable and even if prevention is difficult the position is more hopeful than with most malignant growths.—Smoking, *Tubercle*, December, 1958.

ECHINOCOCCUS IN MAN AND DOG IN THE SAME HOUSEHOLD IN NEW YORK CITY

Max M. Sterman, M.D.
and
Harold W. Brown, M.D., New York

Recurrent spells of abdominal pain in a woman, on the basis of history, physical examination, laboratory tests, and roentgenography, led to a diagnosis of Echinococcus cyst of the liver. This was confirmed at laparotomy, when the intact cyst was removed. Several months later a second cyst had to be removed. In a second patient, a boy of 16, severe symptoms after a sharp blow on the abdomen were found to have been caused by the rupture of an Echinococcus cyst of the liver. Both patients had visited in Greece, where the parasite is highly endemic, but they had also been in contact with a dog that had been imported from Greece and was found to be infected. Of the laboratory tests used, the eosinophil count was the least useful, since it gave normal figures in both cases. The intradermal Casoni test was more reliable than the complement-fixation test.

Approximately 40 autochthonous Echinococcus infections in man have been reported in the United States.[1] We know of several unreported infections, and recent studies in Mississippi indicate that this parasite is more common than the literature suggests. Records of the New York City Health Department reveal 49 reported Echinococcus infections between 1948 and 1957, the majority among immigrants and several among native Americans who traveled abroad in Echinococcus endemic areas. We found no evidence of a native New York City resident contracting the infection in the city.

Swartzwelder,[1b] in a review of all cases of Echinococcus disease in Louisiana, stated that 10 of the 15 recorded cases occurred in native-born Americans. Unfortunately, he did not give data on residence abroad of this group. He emphasized that infection of the dog with the adult E. granulosus is rare in Louisiana and cited the helminthological study of Hinman and Baker,[2] in which no infection with the adult Echinococcus was found in an examination of 1,315 local dogs. Edney [3] and Franklin and Ward [4] have reported canine infections with E. granulosus in southern United States. The two Echinococcus-infected patients here reported reside in New York City, visited endemic centers of the disease, and owned a dog infected with the adult E. granulosus.

Report of Cases

Case 1.—A 42-year-old American housewife of Greek origin consulted her physician on March 4, 1957, for recurrent pain of two weeks' duration in the right upper quadrant. The patient was born and spent her youth in a small town in Greece where dogs and sheep were numerous, and her family owned a dog from time to time. Since her arrival in New York in 1934, the patient had made three visits to Greece, the first in 1938, for six months, and the other two in 1950 and 1955, for two months each. She denied having had any contact with dogs in New York, except for a puppy which the family had acquired during their last visit to Greece in 1955.

A presumptive diagnosis of hydatid cyst of the liver was made on the basis of (1) a history of residence in an Echinococcus endemic area, (2) a history of Echinococcus disease in a brother, (3) the finding of a palpable, somewhat tender mass in the right upper quadrant, and (4) roentgenographic evidence of a localized area of increased, noncalcific density in the right upper quadrant. The complement-fixation test result was negative on one occasion and doubtful on another.

From the Bureau of Preventable Diseases, New York City Department of Health, and Columbia University College of Physicians and Surgeons.

The hemagglutination test gave a positive result in a serum dilution of 1:10,240. The Casoni skin test gave a negative result when read after 30 minutes. There was no eosinophilia.

The patient was operated on March 15, 1957, and a cyst, 9 cm. in diameter, was removed intact from the liver without seepage or spillage. Its inner wall was translucent, extremely friable, and 0.5 cm. in thickness. On section, the cyst contained cloudy fluid with a whitish, sandy sediment which on microscopic examination revealed innumerable scolices and hooklets of E. granulosus.

Several months later, three weeks after her son's operation (case 2), the patient again noted recurrent pains in her right upper quadrant which radiated to her right shoulder and back. There was no nausea or vomiting. Her abdomen was slightly spastic in the right upper quadrant. The liver edge was not palpable. Casoni intradermal test at this time gave a delayed positive reaction. The white-blood cell count was 6,800 per cubic millimeter, with 2% eosinophils. The complement-fixation test finding was positive (3+), and the hemagglutination test was positive in a serum dilution of 1:160. X-ray examination revealed a cyst in the liver which was not demonstrable in previous films. Thirteen and one-half months after the removal of her first Echinococcus cyst a second cyst, 15 cm. in diameter, was removed from the substance of the liver. Her recovery from the operation was uneventful.

Epidemiologic studies undertaken at the request of the surgeon disclosed that the patient owned a 2-year-old German shepherd dog which was ac-

quired in Salonica, Greece, in July, 1955, when it was 4 weeks old. Inquiry of the owner of the dog as to its dietary regimen prior to its importation revealed that the dog ate "everything, including scraps of meat." The animal remained with the family except for a period of 45 days, during which time it was confined in a New York City veterinary hospital for partial paralysis of its posterior limbs. The dog received the usual vaccinations for rabies and distemper, had been dewormed twice presumably for roundworms, and allegedly has been in good health. We examined two stool specimens of the dog, and both specimens contained Taenia eggs, species unidentified.

As the dog was procured from a highly endemic Echinococcus area, the family was cautioned that the Taenia eggs found in the dog's excreta might be those of E. granulosus. They were urged to take the dog to their private veterinarian for tapeworm therapy and were instructed to alert him of our findings. The dog was dewormed, and specimens submitted to us after the vermifuge were identified as adult E. granulosus. To be safe, the dog was sacrificed but no additional tapeworms were found on postmortem examination.

After the discovery of infection in the dog, epidemiologic studies were extended to known close contacts of the dog, including members of the household, relatives, and neighbors. Eleven persons with contact were interviewed and examined; five of them were household members, and the remainder were neighbors and relatives.

The following epidemiologic data were secured from all contacts: place of birth, travel in endemic areas, contact with dogs in endemic areas, and contact with the infected dog in New York. A Casoni skin test with use of two human cyst fluid antigens of proved potency, complement-fixation test, and x-ray of the chest and abdomen were also done (see table).

Eight of the 11 contacts of the infected dog who were tested gave a negative reaction, and one (case 1) gave successively negative, 2+, and 3+ reactions with the Echinococcus complement-fixation test. Seven of the 11 contacts who had roentgenographic examinations of the chest and upper part of the abdomen gave normal findings. Hemograms were within normal range. There was no eosinophilia. Only one household contact (case 2) gave positive intradermal reaction with two Echinococcus antigens.

Case 2.—The 16-year-old younger son of the owner (case 1) of the infected dog had a hemagglutination test positive in a dilution of 1:10,240. However, findings on physical examination, roentgenogram of chest and right upper part of the abdomen, and Echinococcus complement-fixation test were all negative. His white blood cell count was 9,000 per cubic millimeter, with 4% eosinophils. The boy denied contact with dogs during his two months' stay in Greece in 1950 and 1955 but had very close contact with the family's infected dog for almost two years. His family physician was apprised of our findings and their possible implications.

Eight months after his examination, he received a sharp blow on his abdomen from the elbow of an opponent during a basketball game. He immediately experienced a diffuse abdominal pain which radiated to his right shoulder. He felt faint, perspired freely, and vomited. Within four hours his abdomen became rigid. His hemogram showed the red blood cell count to be 5,200,000 per cubic millimeter, hemoglobin level 105%, and white blood cell count 11,100 per cubic millimeter, with 74% neutrophils, 1% eosinophils, 23% lymphocytes, and 2% monocytes. At operation, a ruptured Echinococcus cyst the size of a small grapefruit, adherent to the liver and gallbladder, was found. The small intestine was inflamed. The cyst was removed and found to contain Echinococcus scolices. The patient's recovery was uneventful. Two weeks after operation his complement-fixation test gave positive results.

Epidemiological and Laboratory Data on Human Contacts with Infected Dog

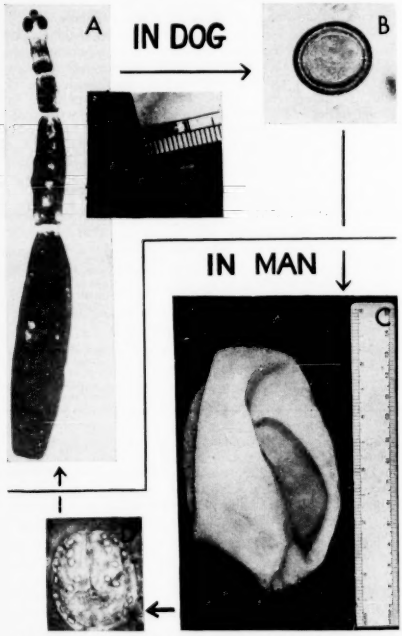
Case No.	Age, Yr.	Sex	Birthplace	Travel History	Dog Contact in Endemic Area	Contact with Infected Dog	Skin Test (Casoni)	Echinococcus Complement-Fixation	White Blood Cell Count, per Cu. Mm.	Eosinophils, %	X-ray of Chest and Abdomen
1	42	F	Greece	New York 1934 Greece 1938, 6 mo.; 1950, 2 mo.; 1955, 2 mo.	Yes	Casual	Negative immediately; positive delayed	Negative; doubtful-positive; positive	...	3	Mass in right upper quadrant; cysts removed from liver 4/15/57 and 5/2/58
2	16	M	New York City	Greece 1950, 2 mo.; 1955, 2 mo.	No	Intimate	Positive immediately	Negative; positive	9,000	4; 6; 1	Negative; cyst removed adherent to liver on 3/27/58
3-12	8-50	6M; 4F	5 foreign; 5 New York City	8 visited Greece	3 yes; 6 no	5 intimate; 5 casual	Negative	7 negative	7,000-11,000	0-3	5 negative; 5 not done

Comment

Of primary interest in this study is the source of the infections of the two patients. Were they acquired in Greece, where the parasite is highly endemic, during the childhood of the patient in case 1; during several visits there later; or in the United States from either their own infected dog or other canine sources? The Echinococcus cysts removed from the patients were approximately 9 to 15 cm. in diameter. The rate of growth of cysts is extremely variable and depends on their site, nutrition, and species of host. In vascular organs, such as the lungs and spleen, growth is often rapid. Edwards noted that a pulmonary cyst grew 2 to 3 in. in diameter in one year. Variations in rate of growth and sudden increases in size have been noted. In the liver of the pig the cyst reaches

a diameter of 2 mm. in two months.[5] An increase of 1 cm. in diameter per year is an average growth rate for hepatic cysts in adult human hosts. Growth rates of 2 to 2.5 cm. in diameter per year have been reported from young children. Extremely slow growth of cysts has been reported, several of which reached a diameter of 2 to 6 cm. in 11 to 23 years. The life cycle of E. granulosus is shown in the figure.

From the foregoing it would appear that the cysts of the two patients could have been from 2 to 15 years old. The patients could, therefore, have acquired the infection from their own



Life cycle of E. granulosis (*A* and *B* refer to part of cycle found in dog and *C* and *D* to that found in man): *A*, adult E. granulosus removed from dog. *B*, E. granulosus egg from dog. This is infectious for man and develops into Echinococcus cyst. *C*, Echinococcus cyst from liver of patient (case 1), opened to show interior. *D*, scolex from cyst which, when eaten by dog, becomes adult tapeworm.

dog or during one of their visits to Greece in 1950 or 1955. The patient in case 1 harbored two cysts approximately of equal size, suggesting that they were possibly acquired at the same time. It seems somewhat unlikely that hepatic cysts of the size harbored by the patients were due to infection from association with their parasitized puppy during the past two years. On the other hand, they both admitted close association with this dog. The third possibility is that the patients acquired the infection in the United States, specifically, New York City. However, all of the 49 infections reported to the New York City Health Department during the past 10 years were in immigrants from endemic areas or Americans who had visited endemic areas. Considering all the evidence available, it is impossible to determine the time and place of infection of the two patients.

The result of the complement-fixation test of the patient in case 1 was negative and "doubtful positive" before the surgical removal of her first cyst and positive 13 months later at the time of the removal of her second cyst. Her Casoni intradermal test prior to her second operation, read at 30 minutes, was negative, but 24 hours later it showed a "delayed positive" reaction. The Casoni skin test of the patient in case 2 one year and also six weeks prior to operation gave an immediate reaction. His complement-fixation test finding was negative one year before operation and strongly positive two weeks after operation, which may be related to the cyst's growth and rupture and the patient's sensitization. It is generally agreed that the intradermal test is a more reliable diagnostic aid than the complement-fixation test. The eosinophil counts of both patients were within normal limits.

Summary

Echinococcus cysts were removed surgically from a woman and her son residing in New York City in whose household lived a dog infected with the adult Echinococcus granulosus. The dog had been imported from Greece.

600 W. 168th St. (32) (Dr. Brown).

Dr. E. Grivelis, St. John's Episcopal Hospital, referred the patient and cooperated in the epidemiologic study. Drs. L. M. Fox and E. Khayat performed pathological studies. Hemagglutination tests were done by Mr. William F. Hutchison, University of Mississippi. Mrs. M. V. Forbes LaRiviere provided laboratory assistance. Dr. K. L. Hussey supplied the photographs.

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CLINICAL NOTES

SIMPLE REGIONAL NERVE BLOCK FOR SURGERY OF THE HAND AND FOREARM

Preston J. Burnham, M.D., Salt Lake City

Injuries to the hand and forearm consistently hold a high place in the incidence of bodily trauma. They often need to be repaired immediately. Unfortunately, the stomach is often full of food and drink or there are multiple injuries which make the use of a general anesthetic a dangerous procedure.

The supraclavicular brachial plexus block has often been employed. However, this block has many disadvantages: First, it is accomplished by pneumothorax and/or phrenic nerve paralysis in 2 to 25% of cases reported.[1] Such a complication might well prove overwhelming to the patient with a severe chest injury. Second, the block is effective in only 68 to 90% of cases.[2] Consequently, general anesthesia is often reluctantly used to augment this block.

The local use of anesthetic agents throughout the field of trauma is to be decried for many reasons, among which are the spreading of infection in an open wound, short duration, use of a toxic amount of anesthetic agent, and, perhaps foremost, the usual uncertainty of results.

There would seem to be a need, therefore, for a type of anesthesia in the arm that would have the following advantages: certainty of result; ease of administration by any physician; minimal danger of systemic toxicity and even of anaphylactic reaction if sensitivity is present; adequacy for major surgical procedures on the hand and forearm, with minor procedures safely performed under regional digital [3] or regional wrist [4] blocks; without danger in the presence of the usual full stomach or of multiple injuries, such as a crushed chest; no such danger as of pneumothorax, inasmuch as both hands and arms are often severely injured; and appropriate for rapid, sure, and safe administration in the event of mass casualties, as in time of severe disasters. The regional block described here appears to meet these requirements.

Regional Anatomy

Figure 1 shows the level at which the block is administered—within 2 cm. of the distal edge of the broad tendon of the pectoralis major. The general pattern of structures in this neurovascular space (see cross-section) reveals the brachial artery to be centrally located and surrounded by all the nerves to the entire forearm and hand. The space is surrounded by a sturdy fascia.

The goal is to bathe all these nerves with sufficient anesthetic solution so that sensory conduction will be completely arrested. It is unnecessary to cause paresthesias by impaling the nerves on the needle or to inject into a nerve.

I have found a 2% solution of lidocaine (Xylocaine) hydrochloride with a 1:200,000 dilution of epinephrine (Adrenaline) to be adequate for even the longest procedures that may last up to four or five hours. In the first 12 cases, I used only a 10-ml. to 12-ml. solution in this neurovascular space

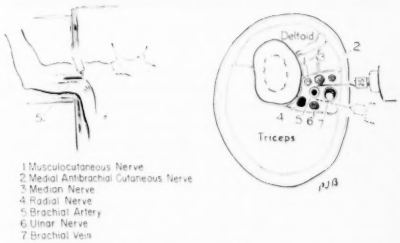

Fig. 1.—Block of great nerves of upper arm, with cross-sectional anatomy.

in the adult with complete anesthesia. In cases 13 and 14, partial failures occurred, probably due to heavy premedication that resulted in a lowering of the systolic blood pressure below 90 mm. Hg, which apparently made accurate identification of the position of the brachial artery somewhat uncertain. In the last 42 cases, I have increased the amount to a total of 16 ml. with complete anesthesia. Relatively few sedatives or narcotics are now given prior to initiating the block.

The shoulder, axilla, and upper arm are first prepared. The patient lies on his back with his arm placed straight out from his shoulder on an adjacent table. The elbow is flexed at 90 degrees and the forearm placed flat on the table. This procedure externally rotates the upper arm and places the neurovascular space uppermost over the humerus. The area is then draped.

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Presented, in part, as a Scientific Exhibit at the 107th Annual Meeting of the American Medical Association, San Francisco, June 23-27, 1958.

The operator wears sterile gloves and stands by the head of the patient so that his palpating fingers come down over the belly of the biceps brachii muscle to find the brachial artery just distal to the pectoralis major tendon (fig. 2).

Fig. 2.—Injection site.

The index finger of the palpating hand is kept on the artery. There is little fat tissue here even in the stoutest patient; hence, a syringe with only a ⅝-in., 25-gauge needle is centered over the artery. The needle is pressed through the skin into the subcutaneous fat, depositing an imperceptible amount of solution constantly. Now the needle is tipped barely to miss the brachial artery and is pushed in until it very clearly "pops" through the fascia. It is pushed on until it is estimated that the point is next to the brachial artery (fig. 1). The plunger is withdrawn partially to test whether the point is in a vessel, while the needle is withdrawn nearly ½ in. If no blood appears, 8 ml. of solution is deposited as the needle is moved in and out over a range of ½ in. to distribute it throughout this part of the neurovascular space.

The needle is then withdrawn from the fascia, but not from the skin, and pressed in to lie near the other side of the artery. Here another 8 ml. is deposited while the needle is moved through a ½-in. range. Each puncture of the fascia is clearly perceived by the operator, even in the thin fascia of children.

It usually requires up to 25 minutes for complete anesthesia to occur. Inasmuch as the success of the block depends on depositing the solution where it will be easily absorbed by the enveloping nerves, the systolic blood pressure should be greater than 100 mm. Hg to make for certain identification of the site of the artery.

Block of Superficial Nerves

Open surgical procedures in the hand and forearm are usually performed with more safety in a bloodless field. I use the Koch-Mason technique of applying a wide blood pressure cuff, high in the upper arm, pumped to a pressure of 280 mm. Hg. Whereas the block arrests conduction in all the nerves to the arm below the elbow, it does not come near the superficial or skin sensory nerves from the cervical plexus, the intercostobrachial nerve, or the perforator branch of the circumflex axillary nerve. Inasmuch as pain arises at the proximal end of the pressure device, I invariably block these sensory nerves with a "ring" type of subcutaneous block with 8 to 10 ml. more of the solution at the level of the block of the great nerves (fig. 3).

Sympathetic Block

The sympathetic block was used twice daily for a week in place of a stellate ganglion block to release arterial spasm. The block alone can be accomplished in 30 seconds without the use of extensive skin preparation or draping. The patient did not on any occasion complain of pain during introduction of needle or solution, as so many do when the stellate ganglion is sought.

Comment

The regional nerve block has been used successfully in 52 patients for major surgical procedures in the hand and for one open reduction of both bones of the forearm. The patients have ranged in age from 2 to 76 years. The children received proportionately less solution, e. g., a total of 8 to 10 ml.

It is my impression that the block of these great nerves in the upper arm should be used in every case—in young or old patients, with good or bad

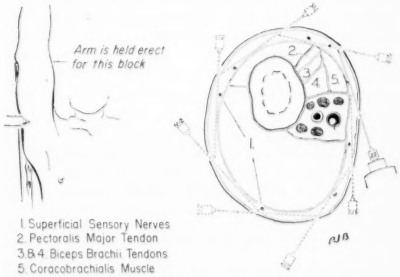

Fig. 3.—Block of superficial sensory nerves of upper arm, with cross-sectional anatomy.

risk, and under elective or urgent conditions. It is a good procedure not only for the operating room but also for the emergency room, for the physician's office, and in the makeshift housing that may

follow disasters. It is easy to perform if the systolic blood pressure is sufficient to make certain the identification of the site of the brachial artery.

508 E. South Temple.

The lidocaine hydrochloride used in this study was supplied as Xylocaine hydrochloride by Astra Pharmaceutical Products, Inc., Worcester, Mass.

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RESECTION OF MULTIPLE METASTATIC PULMONARY LESIONS OF OSTEOGENIC SARCOMA

Alfred T. St. James, M.D., Wallingford, Conn.

Despite the ever-widening horizons of surgery, resection of metastatic malignant lesions, especially multiple metastatic malignant lesions, has not reached a point of full acceptance by the medical profession. The idea is not a new one, for as long ago as 1853 Kroenlein [1] reported a case. Since that time other reports have appeared in the literature, and, as one might expect, the number of reports has increased in recent years. Nevertheless, experience with operation for metastatic malignancy remains both limited and incomplete, especially as to long-term follow-up studies.

At the present time surgical resection of solitary pulmonary metastases is on rather firm ground. Alexander and Haight [2] collected 24 cases from the literature in 1947. Experience at the Mayo Clinic was reported by Hood and associates [3] in 1955; they included a total of 43 cases. Of interest is the fact that their first resection took place in 1941, and 10 years later, in 1951, they had 13 cases. In 41 of the 43 cases, however, the lesions were solitary. In the two that were not solitary, the lesions appeared as satellite nodules rather than as widely separated lesions. Mannix [4] reported use of resection in a patient with multiple pulmonary metastases occurring after osteochondrogenic sarcoma of the tibia. His patient had five metastatic nodules in the basilar segments of the left lower lobe and one in the lingula pulmonis. The patient was treated with basilar segmentectomy and local resection of the lesion in the lingula. At the time of the report, 24 months after operation, the patient was alive and well. A recent case at the Meriden (Conn.) Hospital was similar to the one reported by Mannix, and it is herewith presented.

Read before the annual meeting of the Connecticut Society of American Board Surgeons, New Haven, Conn., Dec. 10, 1957.

Report of a Case

A 16-year-old boy was readmitted to the Meriden Hospital on May 15, 1956, nine months after a high, right thigh amputation had been performed for osteochondrogenic sarcoma. He had been given regular follow-up examinations after the amputation. Chest x-ray findings in January, 1956, were normal. However, a film obtained three weeks prior to the second admission revealed a round, solitary shadow in the right upper lung field (fig. 1). There was no cough, hemoptysis or chest pain. The patient was asymptomatic.

Examination revealed a healthy youth appearing neither acutely nor chronically ill. The temperature was 98.6 F(37 C), blood pressure 120/80 mm. Hg, and pulse rate 72 per minute. There was no dyspnea or cyanosis. The head and neck were normal. There was no cervical lymph adenopathy. The lungs were clear to percussion and auscultation, and the remainder of the physical examination was not revealing with the exception of a well-healed, high, right thigh amputation. Blood studies revealed the hemoglobin level to be 14.3 Gm. per 100 cc. and leukocytes, 9,250 per cubic millimeter, with 56% neutrophils, 1% basophils, 2% eosinophils, 36% lymphocytes, and 3% monocytes. Urinalysis gave normal findings, as did serologic testing. The patient's blood group was B, Rh-positive. An x-ray of the chest revealed a solitary, rounded shadow 2.5 cm. in diameter in the anterior segment of the right upper lobe. The remainder of the lung field was normal. There was no evidence of any pleural fluid.

On May 17, 1956, a right thoracotomy was performed, and a round, hard tumor nodule 2 cm. in diameter was found in the anterior segment of the upper lobe of the right lung. There were also two small nodules in the superior segment of the lower lobe, one posteriorly and the other in the oblique fissure. These each measured 0.5 cm. in diameter. No other nodules were visualized or could be palpated. The lung was entirely free of adhesions. There was no pleural fluid present. Preoperatively, it had been planned to perform right upper lobectomy. The presence of the two nodules in the middle lobe, however, precluded this eventuality, and, accordingly, three local resections were performed of the three metastatic nodules. The chest was closed with underwater drainage. The postoperative course was benign and uneventful, and the patient was ready for discharge on the 11th postoperative day.

Examination of the resected specimens revealed osteochondrogenic sarcoma (fig. 2). After a period of one year, the patient was still free of demonstrable disease.

Comment

The criteria for acceptance of patients for resection of metastatic pulmonary malignancy are not hard and fast. One can only say that small, rather than large, lesions are the more favorable; solitary, rather than multiple, lesions are more favorable; and melanomas, teratoma of the testis, and carcinoma of the rectum are less favorable than others. Generally speaking, sarcomas have a better prognosis than do carcinomas. Jaffe [5] has pointed out that osteochondrogenic sarcoma tends to metastasize to only one lung, whereas osteosarcoma tends to have a bilateral spread, and workers at this hospital are pleased that our case falls into the former group.

In this case, as well as in that of Mannix,[4] it was not recognized preoperatively that the patient had multiple metastatic lesions. Rigler [6] has pointed out that, when favorably located, metastic nodules 2 mm. in diameter have been found on x-ray study of the chest. The smallest lesion in Mannix's patient that had not been visualized in the preoperatively x-ray was 4 mm. in diameter. The lesions not visualized preoperatively in the present patient measured 5 mm. in diameter. Hence, it seems safe to say that, although lesions of only 2 mm. may be visualized, a lesion must be over 5 mm. in diameter before it can be detected with certainty.

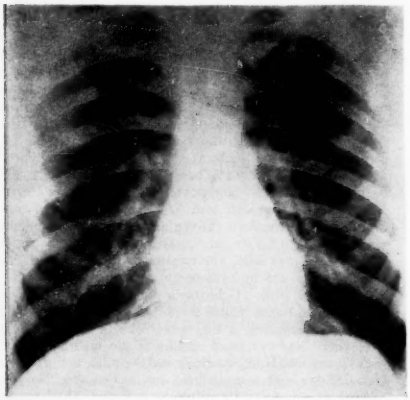

Fig. 1—Chest x-ray, showing coin lesion in right upper lung field.

One need not justify thoracotomy for solitary pulmonary shadows, for not only have favorable results been reported after resection of metastatic disease but also the possibility exists that the shadow may represent a primary bronchogenic carcinoma and that the patient may be cured of his former disease. No doubt had the multicentric nature of the metastases been recognized in this case, operation would have been denied the patient. He

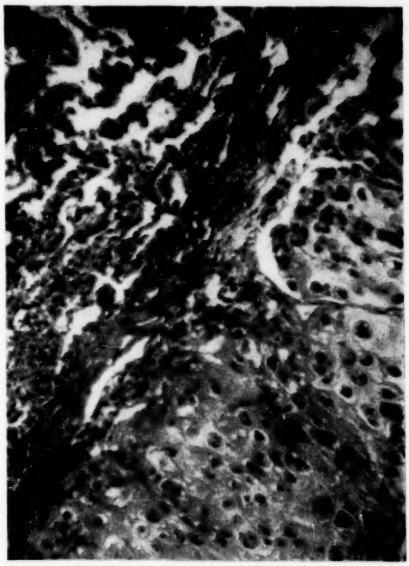

Fig. 2—Microscopic section of resected specimen, showing cartilage-forming metastatic tumor.

is, however, alive, well, and free of demonstrable metastases two years postoperatively. Therefore, a plea is made to extend the limits and concepts of surgery for resection of metastatic lesions to include multiple metastases in favorable cases.

26 Fair St.

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IATROGENIC STIFF SHOULDERS

Robert G. Thompson, M.D.
and
Edward L. Compere, M.D., Chicago

The normal shoulder joint is capable of motion in several directions. The glenohumeral joint contributes the greatest part of the total motion of which the shoulder joint is capable. There is some argument as to the ratio of motion between the glenohumeral and the scapulothoracic articulation, but there is general agreement that at least 120 degrees of motion occur at the glenohumeral joint from adduction to complete abduction of the arm. When the arm is at the patient's side or in complete adduction, the inferior part of the shoulder capsule, of necessity, is quite lax and is believed to fold somewhat in the manner of an accordian. The capsule is obviously stretched out when the arm is at its extreme range of abduction, namely, about 180 degrees. With the arm held in adduction there is a great tendency for adjacent folds of the shoulder capsule to become adherent to one another, particularly if this position is maintained for any length of time. It has been observed that a period as short as two to three weeks of persistent adduction is sufficient to cause severe adhesion formation in the shoulder joint capsule.

It is the habit of a number of surgeons who treat trauma to the upper extremity to immobilize the patient's arm in a sling, a Velpeau dressing, a shoulder spica, a hanging cast, or some other type of fixation. To obtain adequate healing of hand injuries or forearm or elbow fractures, immobilization is required of the affected areas. However, too often the entire arm and shoulder are immobilized for six to eight weeks or longer. Many patients with a completely healed Colles' fracture return to the treating physician complaining of pain and stiffness in the shoulder. They are unable to raise their arm above shoulder level.

Patients will not do what may appear to them to be unnecessary movements. They will not exercise their shoulder joints unless specifically instructed to do so by their physician. Any patient who has a fracture involving the fingers, hand, forearm, or elbow, and is immobilized in a short or long arm cast with or without the use of a sling, should be specifically told on repeated occasions that the arm should be raised above the head several times a day (see figure). If this simple procedure is carried out several times each day, much future suffering and disability can be prevented.

As orthopedic consultants to a rehabilitation center, we have been impressed by the number of stiff shoulders that we have found it necessary to treat after an injury to the hand or arm had healed. A survey of 130 patients with arm or hand injuries admitted to the Liberty Mutual Rehabilitation Center in Chicago from Jan. 1, 1957, to Jan. 1, 1958, revealed a total of 11 patients who had suffered no known injury to the shoulder but were found to have less than normal motion of the shoulder of the arm which had been treated. These patients were questioned, and none recalled that the treating physician specifically instructed them to move the arm at the shoulder through a full range of motion several times each day during the period of immobilization. These patients ranged in age from 34 to 63, with a predominant number above the age of 40 (see table).

Exercise position for fractures of the arm to prevent subsequent stiff shoulder with limited range of movement.

It is a well-known fact that shoulder joints tend to become stiffer with age, particularly above the age of 40. It is therefore doubly important to emphasize to these older patients that they must perform full shoulder motion at least two or three times each day. The exercise of the shoulder should be demonstrated to the patient. Few patients understand what is meant if they are merely told that they should move the arm through a wide or full range of motion. Another exercise, which is also

demonstrated to the patient at the same time, is the way the fingers are to be moved. It is not adequate to simply wiggle the fingers, but a complete fist should be made. If the cast does not permit, it should be trimmed enough to allow full flexion and extension of the metacarpal phalangeal joints.

Treatment of Iatrogenic Stiff Shoulders in Eleven Patients

Age, Yr.	Diagnosis	Interval Between Injury and Admission, Wk.	Shoulder Motion on Admission: Abduction, Degree	Shoulder Motion on Admission: Flexion, Degree	Days of Therapy	Shoulder Motion at Discharge: Abduction, Degree	Shoulder Motion at Discharge: Flexion, Degree
55	Colles' fracture	8	75	110	23	115	160
61	Hand amputation	12	75	80	108	160	180
38	Arm amputation	6	75	95	61	80	100
56	Forearm amputation	12	75	110	17	95	135
47	Forearm burns	20	85	110	22	90	120
54	Fracture, radius & ulna	28	130	155	32	180	180
63	Monteggia fracture	34	110	165	5	115	165
46	Soft tissue arm injury	8	80	95	43	100	125
34	Fracture, dislocated elbow	8	80	105	31	110	130
39	Fracture, radius & ulna	12	100	140	25	100	150
59	Arm amputation	12	85	115	23	100	135

Once a shoulder becomes stiffened, a very difficult therapeutic problem is presented. These patients usually have pain primarily as a result of the limitation of motion. Any attempt to stretch the frozen shoulder will cause severe pain. Because it is painful, most patients resist the therapeutic movement. As can be noted from the table, full shoulder motion was obtained in only one case, and that after vigorous therapy for many days. Several cases of the frozen shoulder syndrome required forceful manipulation of the shoulders with the patient under complete anesthesia in order to restore a satisfactory range of motion.

Summary

The prevention of shoulder stiffness after injuries of the forearm and hand treated by slings or casts or other shoulder immobilization devices requires the active cooperation of each patient. This is accomplished by definitely instructing each patient in a very simple, short exercise of the shoulder, to be performed several times each day. Each of 11 patients in a total group of 130 patients who were treated at the Chicago Rehabilitation Center were found to have varying degrees of stiffness or fibrous ankylosis of their shoulder joints after an injury to the distal part of the arm. This stiff and painful shoulder complication could have been prevented. All patients who have arm injuries which do not involve the shoulder joint should be instructed by the treating physician to carry out definitive exercises of the shoulder joint several times each day. Physicians should try not to commit sins of omission just as they try to avoid sins of commission.

720 N. Michigan Ave. (11) (Dr. Thompson).

Statistical data were prepared by the staff of the Liberty Mutual Rehabilitation Center.

COUNCIL ON DRUGS

NOTICE OF CHANGES IN OPERATION

Descriptions of New and Nonofficial Drugs

In order to further reemphasize that descriptions of drugs published by the Council do not, in any case, imply approval, endorsement, or acceptance, the Council has voted to restate this fact in the introduction to all future monographs and supplemental statements which are published in THE JOURNAL for inclusion in its annual publication, New and Nonofficial Drugs. Although this fact was announced at the time the Council's seal-acceptance procedure was replaced in 1955 by the current evaluation program and has been clearly stated in all subsequent editions of the Council's annual publication, physicians generally should be aware that each drug description is designed to provide fair comment and criticism based on available evidence, whether or not this is considered adequate to establish usefulness. Physicians are urged to read each description to gain a proper appreciation of the Council's views concerning the actions, uses, hazards, and dosage of individual drugs.

More Prominent Listing of Trade Names

In order to make descriptions of drugs more easily identified by physicians who may be familiar with only their commercial names, the Council has voted to place these names in parentheses immediately after the nonproprietary titles of all subsequently published monographs (and in supplemental statements on previously evaluated drugs), instead of at the end or in the text of such descriptions. This change in format is being implemented simultaneously in THE JOURNAL and for the 1960 edition of New and Nonofficial Drugs.

Identification of Commercial Sources

The Council also has authorized the identification of commercial sources of described drugs, of which it has knowledge or is informed, in the index for the 1960 and future annual editions of New and Nonofficial Drugs. The Council voted to indicate such sources parenthetically after all applicable commer-

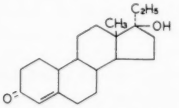
cial names (proprietary or nonproprietary) as they appear in the general index rather than in conjunction with monographs and to provide a separate alphabetic appendix of the complete organizational names and addresses of such sources as a further supplement to this information.

NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based upon available evidence and do not in any case imply endorsement by the Council.

H. D. KAUTZ, M.D., *Secretary.*

Norethandrolone (Nilevar). – 17α-Ethyl-17-hydroxy-19-nor-4-androsten-3-one.—The structural formula of norethandrolone may be represented as follows:



Actions and Uses.—Norethandrolone, introduced commercially in 1956, is a synthetic steroid hormone, which is related chemically and pharmacologically to testosterone. The drug exhibits androgenic properties, which are not as pronounced as with testosterone and its esters. Hence, norethandrolone is not used as an androgen. It does, however, exert a significant anabolic effect, which forms the basis for its clinical use. In laboratory experiments and short-term clinical studies, promotion of protein anabolism as evidenced by a reversal of a negative nitrogen balance has been demonstrated; the anabolic potency of the drug is approximately equal to that of testosterone and its esters. Accordingly, norethandrolone has been employed clinically in situations in which problems of protein catabolism are encountered. These include such conditions or circumstances as preparation for and recovery from surgery, recovery from severe illness, recovery from burns and severe trauma, nutritional care in wasting diseases such as carcinomatosis and tuberculosis, domiciliary care of decubitus ulcer in the chronically ill, and care of malnourished children and premature infants. Although the foregoing uses of the drug might logically follow because of its anabolic effect, they are at present considered theoretical. As yet, there is no evidence that a positive nitrogen balance can be maintained for prolonged periods of time, nor is there any direct evidence that, if this were so, such a therapeutic regimen would shorten convalescence, diminish surgical morbidity, or provide any additional benefits which could not be achieved by an adequate diet alone. Thus, although it can be considered logical to employ norethandrolone for the treatment of conditions characterized by a wasting of body protein, further critical research is necessary to substantiate its ultimate utility for this purpose.

In addition to the property of reversal of negative nitrogen balance already described, under certain circumstances, the drug also effects a decreased loss of calcium; this property suggests its employment in certain conditions in which a greater degree of calcium retention is desirable. To the present time there is no evidence that norethandrolone increases bone age or speeds the closure of epiphyses in prepuberal children.

Norethandrolone, although less androgenic than testosterone and its esters, is capable of producing virilizing effects, especially after large doses or prolonged periods of use. For this reason it is contraindicated in patients with prostatic carcinoma. It may also exert progestational activity, causing endometrial proliferation and withdrawal bleeding in adult women. This reaction is more prone to occur if dosage is high or if therapy is terminated abruptly. Nausea and vomiting, which are seldom severe enough to require discontinuance of therapy, have been reported occasionally. Fluid retention and edema can also occur. The drug should therefore be administered cautiously to patients with demonstrable or incipient circulatory or renal failure and should be discontinued at the first sign of fluid retention. It should not be employed in nephrosis or the nephrotic stage of nephritis since it may effect an increased lipemia in such patients. Because norethandrolone alters electrolyte balance,

it should not be administered to patients with severe burns or trauma during the acute phase of these conditions.

Norethandrolone may alter liver physiology, probably in a manner similar to methyltestosterone, and a few instances of jaundice have been reported. This manifestation is reversible and may not be evidence of true liver toxicity, although it is an indication for prompt discontinuance of the drug. The alteration of liver physiology may result in abnormal values in serum bilirubin, in serum transaminase, and in sulfobromophthalein determinations. However, in the absence of underlying liver disease, other liver function tests are normal. Continuous administration of norethandrolone for periods longer than three months is considered inadvisable, although a second such course may be initiated after a rest period of one month.

Dosage.—Norethandrolone is administered orally or intramuscularly. Although dosage is highly variable, the average daily dose for adults usually ranges from 30 to 50 mg. Amounts as high as 100 mg. per day have been administered, but at this dosage level definite androgenic effects are likely to be encountered. For children, 0.5 mg. per kilogram of body weight is the usual daily oral dose.

Preparations: solution (injection) 25 mg. in 1 cc.; solution (oral) 8.3 mg. per cc.; tablets 10 mg.

G. D. Searle & Co. cooperated by furnishing scientific data to aid in the evaluation of norethandrolone.

Poloxalkol (Polykol).—An oxyalkylene polymer with the following structure:

$$HO(C_2H_4O)_x(C_3H_6O)_y(C_2H_4O)_xH$$

Actions and Uses.—Poloxalkol, introduced commercially in 1958, is a relatively tasteless, nonionic, surface-active agent with actions and uses similar to those of dioctyl sodium sulfosuccinate. After oral administration, the drug lowers surface tension of water and intestinal fluids, thus tending to soften the stool and facilitate elimination. The wetting action of poloxalkol makes it potentially useful for the treatment and prevention of constipation associated with dry, hard stools. Clinical trials, thus far chiefly limited to infants and children, would indicate that the drug is often, but not always, effective in relieving chronic constipation. The action of the drug is neither rapid nor drastic; thus, several days may elapse before a therapeutic effect is apparent. Poloxalkol per se is pharmacologically inert; its fecal moistening effects are due entirely to the detergent-like physical properties of the compound. Although the drug appears to be essentially nontoxic, the possibility that it may increase the absorption of mineral oil or of fat soluble substances in harmful amounts should be borne in mind.

Dosage.—Poloxalkol is administered orally. For infants and children under three years of age, the usual dose ranges from 100 to 200 mg. once or twice daily. For children 3 to 12 years of age, the dose is 200 mg. once to three times daily.

Preparations: solution (oral) 200 mg. per cc.

The Upjohn Company cooperated by furnishing scientific data to aid in the evaluation of poloxalkol.

Use of Phenylbutazone (Butazolidin) in Acute Superficial Thrombophlebitis

The Council has evaluated the clinical use of phenylbutazone for the treatment of acute superficial thrombophlebitis. Although only a few of the available reports of investigations have been well controlled, it is the clinical impression of most observers that the drug exerts beneficial effects in some, but not all, cases. The drug apparently relieves local pain, an action dependent upon its specific anti-inflammatory activity and distinct from the antipyretic or central analgesic properties of the compound. It should be emphasized that phenylbutazone is not intended for thrombophlebitis of the deep veins but should be considered only for selected patients with the acute superficial form of the disease. The Council concluded that further controlled observations are needed to determine its ultimate value in the therapy of this condition as compared with other methods of treatment.

Since the treatment of acute superficial thrombophlebitis involves medication over relatively short periods of time, the danger of drug-induced hematopoietic depression or fluid and electrolyte retention is appreciably reduced. Nevertheless, phenylbutazone should be used cautiously, keeping in mind its known ability to produce serious untoward reactions. Treatment should be discontinued immediately upon the appearance of any toxic effect. (See the monograph on phenylbutazone in New and Nonofficial Drugs.)

In acute superficial thrombophlebitis, which fails to respond to the usual conservative measures, phenylbutazone, 600 mg. per day, may be tried in divided doses for two or three days. If no beneficial results are apparent within 72 hours, the drug should be discontinued. When indicated, 300 mg. per day may be given thereafter for an additional 5 to 7 days, but in no case should therapy be continued longer than 10 days.

The Council voted to amend New and Nonofficial Drugs to describe this additional use of phenylbutazone.

Geigy Pharmaceuticals, Division of Geigy Chemical Corporation, cooperated by furnishing scientific data to aid in the evaluation of the use of phenylbutazone in acute superficial thrombophlebitis.

CHEMICAL LABORATORY

The Chemical Laboratory has authorized publication of the following statement.

WALTER WOLMAN, PH.D., *Director.*

Monographs of tests and assays for new and nonofficial drugs adopted by the Chemical Laboratory of the American Medical Association represent an expression of opinion as to what might constitute adequate tests and assays to serve as a reference guide to those interested in the identity and quality of a new and nonofficial drug.

Completed monographs are published in the journal *Drug Standards* for those interested in the details of the procedures. Monographs on the following drugs have appeared in the November-December, 1958, issue of that journal. The cooperation of the listed pharmaceutical firms that furnished samples and data is acknowledged.

Heptabarbital.....(Geigy Pharmaceuticals)
Hydrocortisone cyclopentylpropionate..(The Upjohn Company)
Mephenesin carbamate.....(E. R. Squibb & Sons)
Penthienate bromide.....(Winthrop Laboratories)
Pyrimethamine.....(Burroughs Wellcome & Co., Inc.)

DIAGNOSTIC PROBLEMS

DIABETES MELLITUS COMPLICATED BY ENTEROCOCCIC MENINGITIS

Clinical Pathological Conference (PM 654-57), Nov. 14, 1957, from the Department of Pathology and the Hektoen Institute for Medical Research of Cook County Hospital, Chicago, presented for publication by Daniel S. Kushner, M.D., and Paul S. Szanto, M.D.

Clinical Data

A 64-year-old man was admitted to Cook County Hospital on May 10, 1957. Information obtained from the patient's wife revealed that he had been taking 10 to 20 units of cloudy insulin daily but that in the last week he had stopped taking insulin and had been eating little because of chills, fever, and malaise. He had been complaining of pain in the rectum and on one occasion "pus" had drained from this area. He had had a cholecystectomy in 1956.

Physical examination revealed a comatose man with Kussmaul respirations and the odor of acetone on his breath. He responded slightly to painful stimuli. His blood pressure was 110/60 mm. Hg, pulse 92 per minute and regular, and respirations 32 per minute. He appeared moderately dehydrated. Purulent drainage emerged from a fistula in ano. No significant additional physical findings were noted. The reflexes were physiological, but the patient had an abnormal response to right plantar stimulation.

Dr. Kushner is Associate Director of Medical Education, Cook County Hospital, and Instructor in Medicine, Northwestern University Medical School; Dr. Szanto is Director, Department of Pathology, Cook County Hospital, and Professor of Pathology, Chicago Medical School.

The urine contained ++++ reducing substance and ++++ acetone. The serum acetone reaction was also strongly positive (++++). The blood glucose level was 1,160 mg. per 100 ml., and the blood carbon dioxide combining power was 12 vol. %. The patient's stomach was aspirated, and 600 cc. of bicarbonate solution was instilled. At 5:30 p. m. treatment was instituted, consisting of 200 units of insulin given intramuscularly and molar lactate intravenously and one million units of aqueous penicillin initially and 400,000 units of penicillin and 0.5 Gm. of streptomycin twice daily. At 8:30 p. m. 400 units of insulin and isotonic sodium chloride solution with 2 Gm. of potassium chloride were given. Urine and serum acetone tests gave positive (+++) results. He seemed slightly improved at 11:30 p. m.; urine acetone was still present (+++), and the serum acetone reaction was ++. He was given another liter of isotonic sodium chloride solution, the stomach was again irrigated, bicarbonate was instilled, and 600 units of insulin was given. By 12:30 a. m. he responded to his name and coughed but was still stuporous. Two liters of 5% dextrose in saline solution with 4 Gm. of potassium chloride was given. His blood pressure was 120/70 mm. Hg, and his urinary output was increasing.

At 5:30 a. m. the urine glucose and acetone and serum acetone tests were all negative. The blood glucose level was 98 mg. per 100 cc., and the carbon dioxide combining power was 42 vol. %. Five per cent solution of dextrose in water was infused. The patient's blood pressure had fallen to 90/60 mm. Hg, but after infusion with arterenol it promptly rose to 110-120 mm. Hg systolic. The urine flow remained brisk. Much mucus was aspirated from the trachea, and by 8 a. m. the patient appeared improved. He was alert and able to take fluids orally. His chest was clear, blood pressure was 140/80 mm. Hg, and he was given 1 pt. (500 cc.) of blood. However, at 1 p. m. he was again semicomatose, and his temperature was 101 F (38.3 C) rectally. Marked nuchal rigidity was present. A lumbar puncture revealed an opening pressure of 135 mm.; the fluid was slightly turbid, Pandy reaction was +++, cell count revealed more than 1,000 polymorphonuclear leukocytes, and a smear showed gram-positive diplococci. He was treated for pneumococcic meningitis with 10 million units of penicillin and 4 Gm. of sulfadiazine by intravenous drip. His abdomen was somewhat distended; intestinal sounds were hypoactive.

By the next day the patient was somewhat more lucid, but the meningeal signs were unchanged. An additional 5 million units of penicillin and 4 Gm. of sulfadiazine were given by intravenous infusion. The hemoglobin level was 73% with 4 million red blood cells, 24,000 white blood cells, 30 polymorphonuclear cells, 60 band cells, 5 lymphocytes, and 5 monocytes; the platelet count was 350,000.

That night the patient had generalized irritability with occasional tremors in his left arm. The paralytic ileus which had developed with abdominal distention seemed improved, and gastric suction was no longer required. However, some generalized tenderness of the abdomen was present. The next morning his condition was unchanged except for some pulmonary congestion. The blood chemical values, which 36 hours earlier had been serum nonprotein nitrogen level, 122 mg. per 100 ml.; creatinine, 2.8 mg. per milliliter; glucose, 600 mg. per 100 ml.; chlorides, 106 mEq. per liter; sodium, 134 mEq. per liter; potassium, 3.2 mEq. per liter; and carbon dioxide, 40 vol. %, were now serum nonprotein nitrogen level, 80 mg.; creatinine, 2.3 mg. per milliliter; chlorides, 126 per liter; sodium, 144 mEq. per liter; potassium, 4.0 mEq. per liter; and carbon dioxide, 46 vol. %. Therapy with fluids and antibiotics was continued, but at 4:30 p. m. the patient died.

Culture of the spinal fluid, reported after death, revealed nonhemolytic Streptococcus (enterococcus) sensitive to penicillin, erythromycin, and tetracycline.

Clinical Discussion

Dr. Daniel S. Kushner: We are confronted with the problem of an elderly diabetic man, ill for one week with chills, fever, malaise, pain, and drainage of pus from the rectal area, who presented in coma with severe diabetic ketoacidosis. Of special interest in the physical examination were the draining fistula in ano and a pathological right plantar response.

He was treated in an interesting fashion which we would have to summarize as ideal, since within 12 hours he was free of acidosis, emerging from coma, and metabolically well. It is of particular interest that he received large doses of insulin, in challenge to the erroneous old concept that insulin is not effective if given in doses exceeding 50 units per hour. Here, insulin in three tremendous doses was highly effective.

The first sign that something was amiss was the development of a hypotensive state after the patient was metabolically well. The first consideration in a man at this age should be cardiogenic shock, due to myocardial ischemia, necrosis, or infarction. However, his subsequent course permits the assumption that this was bacteremic shock.

Next, associated with the fall in blood pressure, the patient again became comatose. He had nuchal rigidity, and the spinal fluid turbidity, increased protein content, and pleocytosis pointed toward a purulent meningitis. It was now apparent that he had had an as yet undefined focus of infection which precipitated his ketoacidosis, with late spread of infection to the meninges. The exact identification of the offending micro-organism now became of the utmost importance, both in establishing the probable primary site of infection and in indicating the most rational therapy. Gram-positive diplococci were observed on smear of the spinal fluid. It would be valuable to know whether the organisms were lanceolate, whether they were, in addition to the pairs, arranged in clusters or in short chains, and whether any occurred intracellularly. Such observations would permit deductions regarding the probable presence of pneumococci, staphylococci, or streptococci respectively. Also, too often we think of intracellular organisms only in relation to Neisserian infection, but any bacterium present in pus will become engulfed by leukocytes; therefore the presence of bacteria within cells leaves no doubt that they are causing infection. After the patient's death, the culture was reported as nonhemolytic Streptococcus (enterococcus), which was sensitive to penicillin, erythromycin, and tetracycline. The sensitivity of this organism to penicillin would be unusual for the enterococcus.

Dr. Metzger: These organisms were resistant to heat and bile insoluble, thus distinguishing them from pneumococci and placing them in the enterococcus group.

Dr. Kushner: Too often gram-positive diplococci observed on smear are assumed by the clinician to be pneumococci. The enterococcus (group D streptococcus) may be spherical, ovid, or even lancet-shaped, but it is typically "berry" shaped, forming pairs, double pairs, and even diplococci or short chains, and it may be alpha, beta, or gamma hemolytic. In addition to its insolubility in bile and resistance to heat, the enterococcus grows in 6.5% sodium chloride solution, also at pH 9.6, and it ferments esculin.

Once we accept the fact that the offending organism was, in fact, enterococcus, which is a fecal organism, we must look for an intra-abdominal focus of infection, from which septicemic spread culminated in purulent meningitis.

Also, from the clinical point of view, a pneumococcic etiology might have been considered unlikely because the patient had no primary pneumococcic focus, no pneumonia, otitis media, sinusitis, or skull fracture, which perhaps 75% of patients with pneumococcic meningitis characteristically exhibit. More important, the patient's onset of illness coincided with a possible focus in the infected fistula in ano. Moreover, while he was being adequately treated for meningitis he developed signs of peritonitis or paralytic ileus, again pointing toward an intra-abdominal focus of suppuration. The increasing abdominal distention initially could be explained by paralytic ileus as occurs with any septicemia or meningitis; but the generalized abdominal tenderness observed later forces one to the conclusion that he had developed peritonitis. He also was azotemic, probably on an extrarenal basis, as one sees in peritonitis and other intra-abdominal suppurative conditions. However, since his problem is one of sepsis, he also might have had abscesses in the kidney, contributing to the azotemia.

We should try to define not only what type of meningitis this diabetic had but how it began, how it spread, and how it caused his death.

The review of enterococcic infections by Rantz and Kirby [1] emphasized the frequency of genitourinary and abdominal primary foci. The patient under discussion could have had a silent ruptured appendix or silent relapsing pancreatitis. We have seen one previous instance of diabetes complicated by purulent meningitis due to a fecal organism, Aerobacter aerogenes, which spread from multiple pancreatic abscesses superimposed upon a chronic relapsing pancreatitis. However, I am inclined to relate the peritonitis in this instance to the rectal abscess or to a hematogenous spread from a systemic infection.

The other characteristics of enterococcic infection are its frequent occurrence in the aged, the prominence of abscesses distributed throughout all the organs, the frequency of endocarditis superimposed upon normal heart valves, and its tendency to produce cerebral, myocardial, and splenic abscesses. The latter is interesting in view of the reported cases of bacterial endocarditis which could not be cured until splenectomy was performed to remove this feeding focus. Also, incidentally, such splenic abscesses may leak into the peritoneal cavity and result in purulent peritonitis. There is nothing to point toward any of these suppurative complications in this patient except, perhaps, for the possibility of multiple brain abscesses in relation to his focal signs of left arm tremors and abnormal right plantar response.

How should this man have been treated? Certainly, 10 to 15 million units of penicillin and 2 Gm. of streptomycin daily have been adequate for enterococcic bacteremia, although still higher doses would be preferable in the treatment of meningitis. The in vitro sensitivity of the enterococcus is of no value in guiding therapy; in fact, it is misleading. Remarkably enough, in this case the organisms were reported to be sensitive to both penicillin and tetracycline. The enterococcus is characteristically resistant to penicillin and sensitive to tetracycline, in the test tube only. Empirically, however, therapy with tetracycline leads to a high rate of failure, relapse, and mortality. On the other hand, paradoxically, a combination of penicillin and streptomycin in high doses leads to recovery in 60% of cases, even in bacterial endocarditis. An explanation lies in the difference between the bactericidal and bacteriostatic end points of the respective antimicrobial agents.[2] Whereas with the tetracycline group the margin between these two levels is very wide, with penicillin and streptomycin it is very slight. Thus, the concentrations necessary to inhibit growth of enterococci are up to 3 units per milliliter for penicillin and 25 mEq. per milliliter for streptomycin. The concentrations required to kill enterococci are 10 units per milliliter for penicillin but still only 25 mEq. per milliliter for streptomycin. The blood levels achievable with penicillin range to 10 units per milliliter at dosage levels of 4 million units per day and to 150 units per milliliter at doses over 20 million units per day. Two Gm. of streptomycin daily produces levels of 25 mEq. per milliliter, and 4 Gm. produces levels ranging to 100 mEq. per milliliter. It is generally considered desirable to achieve a blood level which is 4 to 10 times greater than the bacteriostatic end point. Thus is explained the recommendation for treatment of serious enterococcic infections with doses of penicillin in excess of 12 million units and streptomycin 2 to 4 Gm. daily, approaching bactericidal blood levels. All of these considerations would be much facilitated if the bacteriologist would determine and report the bactericidal rather than inhibitory (bacteriostatic) end points in the in vitro sensitivity studies of the organism. These would provide a more appropriate index to the choice and dosage level of antimicrobial agents.

In summary, I would assume that this patient's primary infection was a perirectal abscess associated with a fistula in ano. From this he developed a dissemination of infection which led to diabetic acidosis. The dissemination may have occurred directly to the meninges, through the vertebral veins of Batson, without septicemia. More likely, a pelvic phlebitis, in relation to a pelvic abscess, resulted in septicemia and hematogenous spread of infection to the meninges, with or without cerebral abscesses. Terminally, peritonitis could have resulted from secondary rupture of a pelvic abscess or rupture of a splenic abscess which occurred in the course of an enterococcic septicopyemia.

Morphologic Changes Encountered in Diabetes Mellitus

Organ	Gross Lesions	Microscopic Findings
Pancreas	Atrophy	...
	...	Hydropic (glycogenic) vacuolization
	Lipomatosis	...
	...	Hyalinization and fibrosis
	...	Degranulation of beta cells
	...	Lymphocytic infiltration of the islands of Langerhans (insulitis)
	Chronic relapsing pancreatitis	Acute and chronic pancreatitis
Liver	...	Fatty metamorphosis
	...	Glycogen in nuclei of hepatic cells (ballooning)
Kidney	Arteriolonephrosclerosis (nonspecific but appears earlier and is more severe than in nondiabetics)	Hyaline thickening of afferent and (characteristically) efferent arterioles
	Glycogen nephrosis	In less than 10% of patients dying of diabetic coma. Glycogen chiefly in cytoplasm of epithelial cells of distal convoluted tubules and Henle's loops
	Fatty nephrosis	Fat deposit chiefly in proximal convoluted tubules
	Intercapillary (nodular) glomerulosclerosis (Kimmelstiel-Wilson syndrome; occurs in long standing cases)	Deposits of homogenous material in central region of glomerular tufts
	Acute and chronic pyelonephritis (nonspecific but quite frequent in diabetes)	...
	Necrotizing papillitis (characteristic but not pathognomonic for diabetes)	Ischemic; suppurative necrosis of tip of renal pyramids
Cardiovascular system	Arteriosclerosis more frequent and more severe in diabetics than in nondiabetics	...
	Marked coronary sclerosis; myocardial infarction	...
Skin	Xanthoma diabeticorum	...
	Necrobiosis lipoidica diabeticorum	Plaques due to homogenization of collagen fibers of dermis
	Insulin lipodystrophy	...
	...	Localized atrophy of subcutaneous tissue
Eyes	Cataract (more frequent in juvenile diabetics than in the corresponding nondiabetic age group)	...
	Retina: small punctate hemorrhages (possibly microaneurysms); hard white exudates; retinitis proliferans	...
Nervous system	Cerebral arteriosclerosis	...
	...	Glia (astrocytic) proliferation in cerebral cortex (possibly due to episodes of hyperinsulinism)
Peripheral nervous system (diabetic neuropathy)	...	Demyelinization of peripheral nerve

We do not make the fullest use of every available facility to get specific bacterial diagnoses in such a case. Among the indications for blood culture are pneumonia, meningitis, and urinary tract infection. If the same organism could have been recovered from the blood as was obtained from the spinal fluid, it would have been most helpful.

Dr. Donald Atlas: This patient was azotemic, with a blood nonprotein nitrogen level of 122 mg. per 100 cc. and a creatinine level of only 2.8 mg. %. This indicates the disproportion between nonprotein nitrogen and creatinine levels that is seen in acute extrarenal azotemia rather than primary renal failure. The creatinine can be excreted through the tubules, whereas the urea is filtered only at the glomerular level. In the presence of an overwhelming infection there is an intense stimulus to nitrogen breakdown far beyond what one would ordinarily expect. This is so intense that Morony recently described a syndrome of pseudouremia due to the overwhelming effects of bacterial toxins on protein metabolism, causing an overwhelming load of nitrogen being dumped on the kidneys.

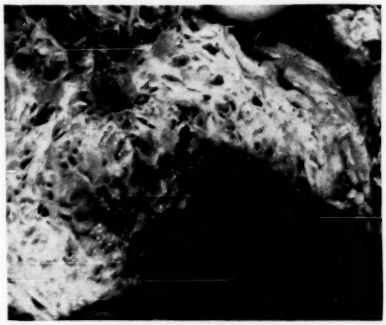


Fig. 1.—Cut section of cystadenoma of pancreas. Note multiloculated structure of tumor.

Dr. Benjamin Gasul: Is the purulent meningitis a certainty? Could this not be a brain abscess or an epidural spinal abscess with rupture into the leptomeninges? The pressure here was not very elevated. Are 1,000 cells sufficient to diagnose a purulent meningitis?

Dr. Kushner: If the brain abscesses were bacterial in origin, their rupture would lead to purulent meningitis anyway.

Dr. Gasul: I agree. It is almost impossible from the data available here to determine the mode of spread of the meningitis.

Clinical Diagnosis.—The final clinical diagnosis was enterococcic meningitis and peritonitis due to pelvic (ischiorectal) abscess secondary to fistula in ano in a diabetic.

Pathological Data

Dr. Paul B. Szanto: The most important morphologic changes which may be encountered in diabetes mellitus include those which are characteristic of diabetes and which are related to the basic metabolic disorder and others which may be associated with diabetes mellitus (see table). Absence of demonstrable pathological lesions in the pancreas does not exclude the possibility of a deficiency of insulin production resulting from an inadequate amount of islet tissue (hypoplasia) as a cause of diabetes. The role of the anterior lobe of the pituitary gland in the pathogenesis of diabetes must also be mentioned. In our material, relapsing pancreatitis is associated with severe diabetes in about 2% of fatal cases. An exacerbation of relapsing pancreatitis may precipitate diabetic coma.

In the case under discussion, the patient appeared well developed and well nourished. The pleural and peritoneal cavities were free of fluid. The heart was moderately enlarged (360 Gm.). The left ventricle was dilated and hypertrophied. Arterio-

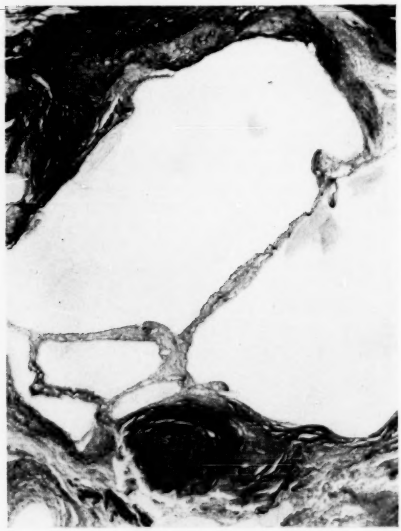


Fig. 2.—Low magnification showing cystic spaces.

sclerotic plaques caused moderate narrowing of the coronary arteries, and foci of fibrosis were found throughout the myocardium.

Bilateral pulmonary edema was present, and a small calcified left bronchopulmonary lymph node was found. The spleen was of normal size (120 Gm.), and its consistency was somewhat decreased. Microscopically, the arterioles were thickened, and the red pulp showed reticulum cell reaction intermingled with polymorphonuclear leukocytes, an acute splenitis reflecting a focal or generalized infection.

A fistula in ano was noted, but there was no evidence of ischiorectal abscess. The peritoneal cavity was free of fluid. Some of the small intestinal

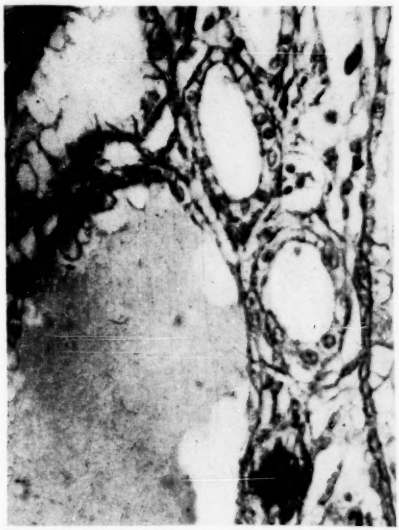


Fig. 3.—High magnification showing epithelial lining of cysts.

loops showed loss of their shiny appearance due to the deposit of minimal amounts of fibrin, as evidence of an early focal peritonitis.

The kidneys were smaller than normal (250 Gm. together). A few scattered glomeruli were fibrosed, but the remainder were normal. The arterioles showed definite thickening.

The pancreas was normal in size (100 Gm.). The head of the pancreas was firm, and its lobular pattern was distorted by fibrous strands of connective tissue. Both the common bile duct and the pancreatic duct were moderately dilated, and each opened separately into the papilla of Vater. Histologically, in the head of the pancreas there was an increase of interlobular and intralobular connective tissue. The few islands of Langerhans were hyperplastic. Starting from the distal portion of, and sharply delineated from, the head of the pancreas, the pancreatic parenchyma was replaced by tumor tissue occupying also the proximal half of the body of the pancreas.

The tumor was multiloculated and consisted of large and small cysts which contained serous or gelatinous material and which were separated by broad bands of connective tissue (fig. 1). Within

the tumor tissue, the pancreatic duct was not identifiable. Histologically, the cysts were separated from each other by slender and broad bands of connective tissue stroma (fig. 2). Some cysts were lined by cuboidal and others by markedly flattened epithelium (fig. 3). In some parts of the tumor,

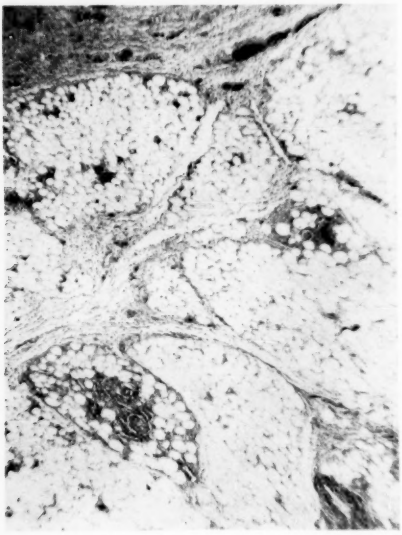


Fig. 4.—Replacement of tail of pancreas by fat tissue.

extensive calcification of the connective tissue was noted. The morphologic appearance of the tumor was that of cystadenoma of the pancreas, although it was not encapsulated. Because of the atypical location and evidence of associated chronic pancreatitis, the possibility exists that this is not a true cystadenoma, but regenerating, proliferating ductal structures as a part of the chronic pancreatitis. Still another possibility is that of a hamartoma. Because of the sharp demarcation, absence of the main pancreatic duct and complete absence within the tumor of any pancreatic structures (islands of Langerhans), the diagnosis of cystadenoma is acceptable. The distal portion of the body and tail of the pancreas were largely replaced by fat tissue (fig. 4) with a few remaining hyperplastic islands of Langerhans.

Finally, a plum-sized abscess was localized to the upper edge of the head of the pancreas. The wall of the abscess cavity was infiltrated by inflammatory cells, and occasionally vascular thrombi were seen.

The liver (1,600 Gm.) showed subacute passive congestion. Microscopically, there was marked reactive proliferation of Kupffer cells. The portal fields were enlarged and infiltrated by polymorphonuclear leukocytes. In the subcapsular part of the hepatic parenchyma, abscesses were found measuring up to 1 to 2 cm. in diameter. The surrounding parenchyma was heavily infiltrated by acute and chronic inflammatory cells. The adjacent branches of the portal vein were occluded by recent thrombi (fig. 5). These were pylephlebitic abscesses secondary to the pancreatic abscess.

The brain was of normal size (1,350 Gm.). The meninges were injected but grossly showed no evidence of a purulent meningitis. Microscopically, there was some meningeal fibrosis, moderate infiltration by mononuclear cells, and small pockets in the subarachnoid space containing polymorphonuclear leukocytes. In view of the clinical data and cerebrospinal fluid alterations, we must assume that

Fig. 5.—Plyephlebitic abscess in liver with thrombotic occlusion of branch of portal vein.

the morphologic picture of purulent meningitis had been altered by antimicrobial therapy. The cerebral vessels showed moderate arteriosclerosis and arteriolosclerosis.

The thyroid was essentially normal. The adrenals were markedly depleted of lipids. The pituitary gland was normal in size and, in one area, showed focal necrosis which is frequently associated with bacterial meningitis.

Pathological Diagnosis.—The pathological diagnosis was cystadenoma of pancreas; chronic relapsing pancreatitis with abscess formation; early peritonitis secondary to extrapancreatic abscess; extreme atrophy of distal portion of pancreas; pylephlebitic abscesses of the liver; and subsiding bacterial meningitis due to enterococcus.

Comment

Non-neoplastic cysts of the pancreas include (1) those due to fibrocystic disease of the pancreas; (2) cysts due to defective development (congenital cysts and cysts due to polycystic disease, with or without association with congenital cysts of the kidney and liver; dermoid cysts; and inclusion cysts from Brunner's glands); (3) retention cysts secondary to obstruction of small or medium-sized pancreatic ducts; (4) pseudocysts, intrapancreatic or peripancreatic (secondary to pancreatitis or trauma); and (5) parasitic cysts. Neoplastic cysts include cystadenoma and cystadenocarcinoma.

In this case, a rare benign tumor of the pancreas, a cystadenoma, occupied the distal part of the head and the greater part of the body of the pancreas. This is a slowly growing tumor which occurs more frequently in females than in males in a ratio of 8:1.[3] A review of 10,000 autopsies in Cook County Hospital revealed only two such cases—this in contrast to Priesel's report of an incidence of 9 cases in 9,000 autopsies.[4] Occasionally the cystadenoma may become malignant. Microscopically, papillary infoldings in the cystic structures of the tumor could be taken as evidence of malignant degeneration. Such infoldings were absent here. Therefore, despite the lack of encapsulation, the tumor in this case is considered to be benign.

This tumor has been associated with diabetes in about 20% of one reported series.[3] The tumor is usually located in the tail and body of the pancreas. The location in the central portion of the pancreas is unusual. The stromal calcification of the tumor in this case might have been demonstrated roentgenographically.[5]

In the case under discussion, the diabetes is explained by a combination of chronic, relapsing pancreatitis involving the head of the pancreas, with a silent cystadenoma, which, by virtue of its location, caused an extensive atrophy of the distal portion of the pancreas. The patient developed an acute exacerbation of the chronic pancreatitis which led to peripancreatic abscess, precipitating diabetic coma. The abscess explains the abdominal tenderness and ileus in relation to a focal peritonitis. The peripancreatic abscess, in turn, led to pylephlebitic abscesses, either of which may have resulted in a suppurative meningitis. We have previously observed the combination of relapsing pancreatitis and purulent meningitis caused by a fecal organism (Aerobacter aerogenes) as a result of hematogenous spread from pancreatic abscesses. Whenever a patient in diabetic coma develops symptoms of meningitis, this possibility should be considered.

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HYALINE MEMBRANE DISEASE.—The recognition of hyaline membrane disease is . . . of recent origin. It is almost entirely confined to premature infants, is particularly common after caesarean birth, and is usually fatal. The exact cause is not known, but experimental work suggests that oxygen may play an important part. The latest report, from Sweden, by R. Berfenstam and colleagues, suggests that excessive oxygen may act by diminishing the ciliary activity in the bronchial tree and thereby favor the retention of the material forming the hyaline membrane. In rabbits exposed to oxygen in 70-80% concentration for 48 hours the ciliary action was both quantitatively and qualitatively reduced. Berfenstam and colleagues suggest that premature infants, adapted to low oxygen tension in utero, may show evidence of oxygen toxicity at relatively low concentrations in extrauterine life, and they stress the necessity for determining what level of oxygen concentration is safe for such infants in their earliest days after birth. They also found experimentally that excessive oxygen caused vascular damage with increased capillary permeability, and the resulting exudate probably furnished the main part of the hyaline membrane.—Physical Activity and Coronary Disease, Editorial, *British Medical Journal*, Dec. 20, 1958.

THE JOURNAL
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NASAL MEDICATION

Physicians who prescribe topical nasal medication frequently assume that this type of medicament should always react on nasal mucous membranes in a predictable manner; they are unaware that, while nasal medication is pharmacologically constructed to exert a constant and predictable effect, the nasal environment into which topical nasal medicaments are introduced is far from constant and is continuously subject to change. The degree of response between individual noses given the same dosage of a drug may differ, and the response itself may vary from nose to nose and from time to time.

Intranasal medication has definite indications and purposes. If these are recognized and if the underlying nasal pathological condition is properly evaluated and the medicament employed judiciously used, satisfactory clinical responses are frequently elicited. Nasal vasoconstrictors, for example, are among the more important drugs available for use in the nasal cavity. Nasal vasoconstrictors relieve nasal congestion for varying periods of time, promote comfort, improve nasal ventilation, and, when rationally used, aid in promoting adequate drainage from paranasal sinuses by opening obstructed ostia. Although these drugs afford symptomatic relief only, even temporary relief from the discomfiture of nasal obstruction due to the common cold, sinusitis, and nasal allergy is welcome to distraught patients.

The problem of producing new sympathomimetic amines is of great importance and has been slowly gathering attention in the pharmaceutical world. Various nasal vasoconstrictors in combination with various sulfonamides, antibiotics, antihistamines, and, more recently, with steroid hormones, have been introduced. Some of the available combinations include such antibiotics as polymyxin B sulfate, gramicidin, and neomycin. While some forms of combined intranasal liquid medication have their ardent supporters, other investigators view combination liquid nasal solutions with restraint.

In order to use nasal medication in clinical practice effectively and intelligently, it is necessary to relate these medicaments to various aspects of the nasal environment. Nasal medication should be regarded not only in terms of its inherent pharmacological properties but also in terms of its local effect on nasal and sinus mucous membranes, ciliary motility, nasal pH, and its systemic effect on the body itself. Effective nasal medication not only should do what the prescribing physician hopes to accomplish in the patient's nasal cavity without causing injury to the mucous membranes but also should instigate no harm elsewhere in the body.

Fabricant[1] has demonstrated that nasal vasoconstrictors with an unusually high alkaline pH value may disturb the normal, slightly acid pH level present in clinically normal nasal passages, enhance irritation of the nasal mucous membranes, and postpone the return of the nasal mucous membranes from a pathological alkaline status to a normal, slightly acid status. During an attack of acute rhinitis, acute sinusitis, and the more active stages of allergic rhinitis, the use of a nasal vasoconstrictor that lowers the abnormal alkaline nasal pH found in these entities to a normal, slightly acid pH level between 5.5 and 6.5 in adults, or 5.0 and 6.7 in infants and children, in short, a true physiological nasal pH, is most desirable for efficacious therapy.

The increasing use of orally administered sympathomimetic amines for the relief of nasal congestion constitutes a revival of an old concept. Support for the efficacy of oral nasal decongestion as a therapeutic procedure is derived from various sources. As with topical nasal vasoconstrictor medication, orally given nasal decongestants can be usefully employed in all nasal conditions in which decongestion is desirable. One advantage displayed by topical nasal vasoconstrictor medication is the rapidity with which decongestion occurs in contrast to the 15 to 30 minutes required for oral medication to take effect. Contrariwise, the advantage of orally given nasal decongestants is that they cause shrinkage of all nasal and sinal tissues rather than part of them, as is the case in conventional topical administration. Clinical experience suggests that the oral nasal decongestion approach will assume a position alongside that of topical nasal decongestion as an efficacious procedure for the relief of the stuffy nose. Orally given nasal decongestants can either be used as adjuvants to topically given medicaments or in their stead.

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THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

You may have received in the mail, or will shortly, a leaflet with your A. M. A. membership card called "Science and Service to Humanity—your concern and the concern of the A. M. A." The pamphlet describes the meaning of your A. M. A. membership.

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Your patients can depend on the A. M. A.'s constant promotion of better health and its search for the best solutions to problems involving medicine and public welfare. Because health is priceless, your help and continuing interest are required to carry on the work of your A. M. A.

GUNNAR GUNDERSEN, M.D.
La Crosse, Wis.

ORGANIZATION SECTION

SECTION CENTENNIALS, ATLANTIC CITY MEETING

At the Louisville, Ky., session of the American Medical Association in 1859, six sections of the Association were formed. Some of these sections were eventually combined or divided. The Section on Surgery, General and Abdominal was originally called Section on Surgery. It was given its present name in 1914. The Section on Internal Medicine was first the Section on Practical Medicine and Obstetrics. In 1873 it was split into (1) Section on Practical (Practice of Medicine) Materia Medica and Physiology (the terms Practical Medicine and Practice of Medicine were used interchangeably for many years) and (2) Section on Obstetrics and Diseases of Women and Children. In 1946 it became the Section on Internal Medicine. The Section on Obstetrics and Diseases of Women and Children in 1911 became the Section on Obstetrics and Gynecology.

The Section on Experimental Medicine and Therapeutics started out as the Section on Chemistry and Materia Medica. In 1905 it became the Section on Pharmacology and Therapeutics, and in 1941 it was given its present name. The Section on Pathology and Physiology was originally the Section on Anatomy and Physiology. It was redesignated the Section on Pathology and Physiology in 1901. The Section on Nervous and Mental Diseases was first called the Section on Medical Jurisprudence and Hygiene and received its present name in 1900. All of these section names underwent various changes not listed. The section that underwent the greatest number of changes was the Section on Preventive Medicine. Two sections were formed in 1859, to which the present section is traced.

1859 Section on Meteorology, Medical Topography and Epidemic Diseases.
1870 Section on Climatology and Epidemics.
1871 Section on Meteorology and Epidemics.
1859 Section on Medical Jurisprudence and Hygiene.
1865 Section on Medical Jurisprudence, Physiology and Hygiene.
1872 Section on State Medicine.
(This new Section was combined with the above two sections the next year.)
1873 Section on State Medicine and Public Hygiene.
1879 Section on Medical Jurisprudence, Chemistry, Psychology, State Medicine and Public Hygiene.
(This terminology was too unwieldy, hence it was shortened the next year.)
1880 Section on State Medicine.
(There was controversy over this terminology.)
1900 Section on Hygiene and Sanitary Science.
1908 Section on Preventive Medicine.
1909 Section on Preventive Medicine and Public Health.
1922 Section on Preventive and Industrial Medicine and Public Health.
1957 Section on Preventive Medicine.

These seven sections of the Scientific Assembly will observe centennials at the Atlantic City meeting, June 8 to 12, 1959, with appropriate ceremonies. Among the guests who have already accepted invitations to the meeting are three from England. Mr. Andrew Claye, president of the Royal College of Obstetricians and Gynecologists, will address the Section on Obstetrics and Gynecology. Dr. J. N. Morris, London Hospital Research Laboratories, will be the centennial guest of the Section on Experimental Medicine and Therapeutics, while Dr. R. R. Coombs, University of Cambridge, will be the guest of the Section on Pathology and Physiology. Other sections are planning features which will be announced soon.

NEW APPOINTMENTS FOR DRS. TURNER AND WIGGINS

Dr. Edward L. Turner was named Director of the new A. M. A. Division of Scientific Activities and Dr. Walter S. Wiggins was named to succeed Dr. Turner as Secretary of the Council on Medical Education and Hospitals. In announcing the staff changes Feb. 10, Dr. F. J. L. Blasingame, Executive Vice-President, noted that the new Division includes the Councils on Mental Health, Scientific Assembly, and Medical Education and Hospitals; the American Medical Education Foundation; and the Department of Therapy and Research.

Prior to joining the A. M. A. Council staff in 1953, Dr. Turner was dean of the University of Washington School of Medicine, Seattle, which he helped organize after leaving a private practice in Bradford, Pa. He also served as president of Meharry Medical College at Nashville, Tenn. (of which he is still a trustee), and was a professor of physiology and head of the department of medicine at the American University of Beirut in Lebanon. Currently he is Secretary of the American Medical Education Foundation, consultant or advisor to a number of governmental and philanthropic organizations concerned with health and medical education, associate trustee of the University of Pennsylvania, a director of the National Internship Matching Program, and on the planning committee of the Second World Conference on Medical Education.

Dr. Wiggins joined the Council on Medical Education and Hospitals as Associate Secretary in 1954. Previously he had been assistant dean, State University of New York College of Medicine at Syracuse, director of the Syracuse Medical Center Tumor Clinic, and instructor and assistant professor of medicine at the Syracuse University College of Medicine.

MEDICAL NEWS

COLORADO

Students Receive Scholastic Awards.—Fifteen University of Colorado School of Medicine students received awards for scholastic excellence at an honor convocation Jan. 22 on the Medical Center campus, Denver. Dean Robert J. Glaser presided. The awards were made by members of the School of Medicine faculty representing the various categories involved. The convocation was combined with the annual lecture sponsored by Alpha Omega Alpha, honorary medical fraternity, and the speaker was Dr. Robert A. Moore whose subject was "Devotion to Excellence." Dr. Moore is president of the New York University's Downstate Medical Center and is dean of its medical school. These students received awards:

Noel C. Sorrell, Albuquerque, N. M.; Arnold Silverman, Bronx, N. Y.; John Moxley, Denver; Gerald Mayfield, Las Cruces, N. M.; Thomas J. Campbell, Grand Junction; Lawrence McKinnis, Boulder; Neil Riggenbach, Monte Vista; Donald J. Stouder, Englewood; Robert W. Thompson, Lander, Wyo.; William Droegemueller, Kersey; Hillmer A. Fonken, Ft. Collins; Jo Anne Brasel, Boulder; Eveline E. Schneeberger, Denver; Watson Bowes Jr., Denver; and David L. Bowerman, Victor, N. Y.

The awards are all monetary, in varying sums, and some apply on tuition.

Russian Surgeons Visit Denver.—Three of Russia's outstanding academic surgeons were guests of their U. S. counterparts in Denver during the 20th annual meeting of the Society of University Surgeons, Feb. 12-14. Arrangements for the visitation were completed as part of the U. S.–U. S. S. R. exchange agreement of medical lecturers between the two countries. The Russian visitors are: Dr. Boris Petroff, professor and chief surgeon, the Skilfosowsky Institute, Moscow; Dr. Fedor Uglov, professor and chief surgeon, First Medical Service, Leningrad; Dr. Boris Ositov, professor and chief surgeon, Institute of Postgraduate Study, Moscow. Accompanying the Russian surgeons on their trip from New York was Dr. Henry T. Randall, chairman, department of surgery, Memorial Hospital, New York City, and president-elect of the Society of University Surgeons. The Russian surgeons also visited other U. S. medical institutions, where they delivered lectures, including Baylor University Medical School, Houston, Texas; University of Minnesota, Minneapolis; Mayo Clinic, Rochester, Minn.; Western Reserve University, Cleveland; the National Institutes of Health, Washington, D. C.; and the Johns Hopkins University, Baltimore.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

ILLINOIS

Quincy Physicians Aid Education.—The Swanberg Kiwanis Foundation, joint sponsor with the Kiwanis Club of Quincy of the Quincy Major Learning Program, has received the 1958 B. V. D. Community School Improvement Award for the East Central Region of the United States. These awards are presented annually by the B. V. D. Co., of New York. The Quincy Major Learning Program was declared by the judges to be "the most outstanding citizens' effort for the betterment of community schools in the nine-state region of Alabama, Illinois, Indiana, Kentucky, Michigan, Mississippi, Ohio, Tennessee, and Wisconsin, for 1958." The award was presented Jan. 19. The Quincy program, initiated by the Swanberg Kiwanis Foundation of the Kiwanis Club of Quincy in 1956, is devoted "to early identification of the superior and talented students in the high schools of Quincy and Adams County and their guidance and motivation to seek a college education." Last year the Kiwanians induced the Quincy and Adams County physicians, through the Adams County Medical Society and the Swanberg Medical Foundation, to establish Academic Scholarship Achievement Awards whereby "talented high school seniors are recognized for scholarship achievement, especially in academic subjects."

Chicago

Clinical Meeting.—The annual Clinical Conference of the Chicago Medical Society will be held at the Palmer House, March 2-5. Thirty-three half-hour lectures, a panel discussion, a clinical-pathological conference, and medical color telecasts are planned. Out-of-state participants include the following physicians:

Edwin H. Ellison, Milwaukee; Edward C. Mann, William T. Foley, and Robert H. Kennedy, New York City; John C. McClintock, Albany, N. Y.; E. V. Allen, Rochester, Minn.; Schuyler G. Kohl, Brooklyn; Julius L. Wilson, Philadelphia; William R. Sandusky, Charlottesville, Va.; John H. Ebersole, Waterford, Conn.; J. Walter Wilson and A. Estin Comarr, Los Angeles; John R. Haserick, Cleveland; Russell S. Fisher, Baltimore; John P. McGovern, Houston, Texas; Ted F. Leigh, Atlanta, Ga.; Norman F. Miller, Ann Arbor, Mich.; David M. Hume, Richmond, Va.; and Stewart Wolf, Oklahoma City, Okla.

A trauma demonstration, instructional courses, and scientific and technical exhibits are arranged. For information write the Chicago Medical Society, 86 E. Randolph St., Chicago 1.

Personal.—Dr. Edward F. Lis, director of the Center for Handicapped Children at the University of Illinois Hospital, has been appointed acting director of the university's state-wide division of services for crippled children. The appointment fills the vacancy created Jan. 10 by the death of Dr. Herbert R. Kobes, division director in Springfield.——Dr. Eleanor M. Humphreys, who has been associated with the department of pathology, University of Chicago, since 1926, has been made professor emeritus and consultant. For 11 years prior to retirement Dr. Humphreys was in charge of surgical pathology. The American Medical Women's Association honored Dr. Humphreys as the "Woman of the Year" for 1958.——Dr. Ernst T. Mörch, professor of surgery and director of the section on anesthesiology at the University of Chicago for the past six years, has been made chief and professor of anesthesiology at Cook County Hospital, Chicago, effective Dec. 1. Dr. Mörch, who received the degree of doctor of medicine in 1935 and the degree of doctor of philosophy in 1942 both from the University of Copenhagen, received postgraduate medical training in surgery in Denmark 1935-46.

KENTUCKY

County Officers Conference.—Third-party medicine will be the topic highlighted at the ninth annual County Society Officers Conference of the Kentucky State Medical Association in Lexington March 26. Mr. Hugh Brenneman, Lansing, public relations counsel for the Michigan State Medical Society, will moderate a panel on problems developing in the third-party field. Panelists will include Dr. Ernest B. Howard, Chicago, Assistant Executive Vice-President of the American Medical Association; Leslie Hodson, Chicago, legal counsel for the A. M. A.; and Dr. Donald Cass, Hollywood, delegate to the A. M. A. from California. Luncheon speaker will be Dr. Russell B. Roth, Erie, vice-chairman, board of trustees, Medical Society of the State of Pennsylvania.

MASSACHUSETTS

School Health Conference.—The Massachusetts Conference on School Health will be held at the Statler Hilton, Boston, March 18. Dr. Charles C. Lund, president, Massachusetts Medical Society, will open the meeting followed by a talk by Dr. Thomas F. Reilly, chairman, Committee on School Health, Massachusetts Medical Society. The program includes the following:

Necessary Elements for Health Evaluation of Children, Dr. Maurice M. Osborne, Jr., director of child health, Brookline Health Department.

A Program of Physical Education, Mr. Reagh C. Wetmore, head, department of physical education, Phillips Andover Academy.

Recognizing the Orthodontic Problem, Milton J. Meyers, D.M.D., instructor, Tufts University Dental School.

Two panels are planned: "Eye Problems in the School Child," with Drs. Richard B. Pippitt, Thomas Cavanaugh, and Thomas P. Cronin Jr., and "Emotional Disturbances," with Dr. Richmond Holder, Dr. John A. Davies, and Mr. Charles K. Cummings, director of guidance, Weston Public Schools.

MISSOURI

Hospital Alumni Meeting.—The St. Louis City Hospital Alumni Association will hold its 71st annual meeting Monday, March 9, at the Le Chateau Restaurant, 10405 Clayton Road, St. Louis County. The American College of Surgeons will be meeting in St. Louis at the same time, and the alumni of the hospital will be able to attend this annual dinner party. For information write Dr. Shale M. Rifkin, Suite 830, 3720 Washington Blvd., St. Louis 8.

NEBRASKA

Physicians Meeting in Omaha.—The 13th annual regional meeting of the American College of Physicians for Nebraska will be held March 7 at the Sheraton–Fontenelle Hotel, Omaha. The program includes the following papers:

Macroglobulinemia: A Case Under Study for Three Years, Dr. John C. Thompson, Lincoln.

Refractory Anemia Responding to Androgen Therapy, Dr. Henry J. Lehnhoff Jr., Omaha.

New Ideas for Cardiac Exercise Tests, Dr. F. Lowell Dunn, Omaha.

Ammonia Metabolism in Hepatic Coma, Dr. Joseph M. Holthaus, Anthony J. Barack, Ph.D., and Fred L. Humoller, Ph.D., Omaha.

Whipple's Disease: A Case Report with Unreported Findings, Drs. Robert A. Youngman and Edward D. Zeman, Lincoln.

Dr. Dwight L. Wilbur, San Francisco, president, American College of Physicians, will present "Some Considerations of Functional Gastrointestinal Disorders" at 3:45 p. m. and will speak on "The Third Person in Medicine" at the banquet 6:30 p. m. For information write Dr. Edmond M. Walsh, 5002 Dodge St., Omaha.

NEW JERSEY

Dr. Nenno Named Department Director.—The appointment of Dr. Robert P. Nenno as professor and director, department of psychiatry, Seton Hall College of Medicine and Dentistry, has been announced. In 1953-1957, Dr. Nenno was assistant professor and assistant director of the department of psychiatry, Georgetown University School of Medicine, Washington, D. C. He has served as

consultant at Georgetown University Hospital, where he initiated the retarded children's clinic. Dr. Nenno is a diplomate of the National Board of Medical Examiners and the American Board of Psychiatry and Neurology.

Conference on Child Amputees.—In conjunction with the 10th anniversary of the Kessler Institute for Rehabilitation, the biannual Congenital Child Amputee Conference and Clinic will take place at West Orange, N. J., May 2. After the 9 a. m. registration, the morning program will consist of an educational and orientation session. Dr. Henry H. Kessler, medical director, will discuss "Congenital Malformations and General Principles of Rehabilitation of the Congenital Amputee." Demonstrations will be given of treatment techniques and prosthetic devices employed in rehabilitation of upper and lower extremity child congenital amputations. Documentary films of rehabilitation procedures used in specific cases will be shown. Clinical examinations will be held in the afternoon. This free diagnostic service is available to congenital amputee children through medical referral. The conference is open to physicians, nurses, limb makers, therapists, and other rehabilitation personnel without charge. Advance registration is requested with Mrs. Lucile Gould, Kessler Institute for Rehabilitation, West Orange, N. J.

NEW YORK

Dr. Witebsky Named Dean in Buffalo.—The University of Buffalo has named Dr. Ernest Witebsky as the new dean of its School of Medicine. Dr. Witebsky has served as acting dean of the medical school since the death last February of the former dean, Dr. Stockton Kimball. He is also professor and head of the department of bacteriology and immunology. Dr. Witebsky received special honors for his research last June from the University of Freiburg, Germany. He holds an M.D. degree from the University of Heidelberg and was a member of the faculty of that university from 1929 to 1933. Dr. Witebsky, one of the original organizers and chairman of the International Society of the Hematology Program in Buffalo in 1948, is a bacteriologist and serologist at the Buffalo General Hospital.

New York City

Lecture on Trigeminal Neuralgia.—Dr. Francis C. Grant, emeritus professor of neurological surgery, University of Pennsylvania School of Medicine, will present the Charles A. Elsberg Lecture May 19th, 8:30 p. m., at the New York Academy of Medicine, 2 E. 103rd St. Dr. Grant has chosen for his subject "Trigeminal Neuralgia."

Personal.—Dr. Saul S. Samuels has been elected founding president of the International College of Angiology.——Dr. Samuel A. Thompson, appointed to the staff of New York Medical College in 1923 as instructor in surgery and named associate professor of surgery in 1938, has been appointed chief of the section of thoracic surgery at New York Medical College, Flower and Fifth Avenue Hospitals.

Train Hospital Personnel to Fight Fires.—A fire-fighting training program given to hospital employees is presently being conducted by the Jewish Chronic Disease Hospital, Brooklyn. Inaugurated in July under the direction of Mr. Eddy Charles, the hospital's director of building services, 30 hospital employees at a time are given complete training in the fighting of fires at the hospital. The program includes actual demonstrations with fire and fire-fighting apparatus used in extinguishing fires. This includes asbestos blankets, fire extinguishers, carbon dioxide, soda and acid. At each monthly session, participants show what they have learned by participating in fire extinguishing. Discussions and training on fire prevention with specific demonstrations with various types of equipment are carried on by Mr. Charles. Each new employee takes the course within one month after joining the hospital staff. More than 200 members of the hospital's staff have received training in this program.

Dr. Stone Takes World Tour.—Dr. Abraham Stone, director of the Margaret Sanger Research Bureau, 17 W. 16th St., left Feb. 6 on a trip around the world in connection with the problems of population and family planning. Dr. Stone flew to New Delhi, India, to take part in the seventh International Conference of the International Planned Parenthood Federation, of which he is a vice-president. He visited Moscow en route to New Delhi. At the close of the conference, he will remain in India at the invitation of the Indian Health Service, spending three or four weeks observing and studying the work of the Indian planned parenthood programs and consulting with health officers and clinicians. Dr. Stone was also invited by the Family Planning Association of Pakistan to participate in a seminar and to hold training seminars in Dacca and Lahore. In West Pakistan, he will be a guest of the Ministry of Health. During his return trip to the United States, Dr. Stone plans to stop at Taiwan, in the Philippines, and in Japan.

PENNSYLVANIA

Conference on Experimental Psychiatry.—On March 5, 6, and 7, the Western Psychiatric Institute and Clinic will sponsor a Conference on Experimental Psychiatry as part of Pittsburgh's year-long bicentennial celebration. The following men will participate: Dr. John D. Benjamin, Ray L. Birdwhistell, Ph.D., Dr. Jack R. Ewalt, Dr. Robert H. Felix,

Dr. Ralph W. Gerard, Dr. Francis J. Gerty, Dr. Roy R. Grinker, Ernest R. Hilgard, Ph.D., Heinrich Klüver, Ph.D., Dr. Lawrence S. Kubie, Dr. Alexander H. Leighton, Dr. William Malamud, Dr. Amedeo S. Marrazzi, Dr. Warren S. McCulloch, and Robert A. Patton, Ph.D. For information write Dr. Henry W. Brosin, Director, Department of Psychiatry, University of Pittsburgh School of Medicine, 3811 O'Hara St., Pittsburgh 13.

Philadelphia

Conference on Gerontology.—The research facility and medical staff of the Home for the Jewish Aged, Philadelphia, for the past three years have been holding monthly conferences in Gerontology. On April 12, 10 a. m., Dr. Werner Henle, professor of virology, University of Pennsylvania School of Medicine, will present "Respiratory Viruses in the Geriatric Patient."

TEXAS

Neurological Meeting in Houston.—The Houston Neurological Society is having its seventh annual scientific symposium meeting March 12-14 in the auditorium of the Jesse Jones Library Building in the Texas Medical Center, Houston, with registration beginning at 8 a. m., March 12. The annual banquet will be at 6:45 p. m., March 13, in the Emerald Room of the Shamrock–Hilton Hotel, with Charles M. Pomerat, Ph.D., professor of cytology, University of Texas Medical Branch, Galveston, as guest speaker. His subject will be "The Mediterranean—Source of Cultural Inspiration." The scientific program will be a symposium: "Pathogenesis and Treatment of Cerebrovascular Disease," to extend over three days and consist of the following parts: "Anatomy," "Occlusive Disease," and "Intracranial Hemorrhage." There will be 20 participants on the program, and the symposium moderator will be Dr. William S. Fields, chairman, department of neurology, Baylor University College of Medicine. Registration fee is $5. Physicians and others interested in basic neurologic sciences are cordially invited. For information, write Dr. Claude Pollard Jr., Secretary-Treasurer, Houston Neurological Society, 437 Hermann Professional Bldg., Houston, Texas.

WEST VIRGINIA

Research Foundation Acquires Kanawha Hospital.—Dr. Gustavus B. Capito, of Charleston, has turned over to the Charleston Foundation for Medical Research and Education 60% of the stock of the Kanawha Valley Hospital and Kanawha Valley Hospital Building Association. The board of trustees of the recently organized foundation includes John M. and Charles Capito, nephews of Dr. Capito; an accountant; a bank president; and two attorneys, all of Charleston. Dr. Capito announced recently that the Kanawha Valley Hospital would become a nonprofit institution after nearly 50 years of operation as a privately owned stock corporation. Stockholders will receive the appraised value of their stock from future profits. The value of the stock turned over by Dr. Capito to the foundation was not announced; however, the fund will be held in trust and the income from it applied by the trustees to fulfill the purposes of the foundation. Dr. Capito has indicated that in the field of research to be undertaken by the foundation, due consideration be given to the new four-year school of medicine at West Virginia University. He has requested that at the present time local benefits be given priority, particularly research into aid for the medicaly indigent. A trust agreement between Dr. Capito and the trustees states that the purpose of the foundation will be "to conduct research in the fields of medicine, science, education and related subjects." Dr. Capito, who celebrated his 81st birthday Jan. 25, will remain as hospital counselor without compensation. He formerly served as president and medical director.

GENERAL

New England Allergists Meet in Boston.—On March 25 the New England Society of Allergy will hold its annual meeting in Boston. Sessions will be held at Longwood Towers. The program committee has announced that it will consider papers for presentation submitted by members of the society. The business meeting is planned for 7:30 p. m. For information write the New England Society of Allergy, 300 Longwood Ave., Boston.

Invite Requests for Eye Research Grants.—The Research Committee of the National Society for the Prevention of Blindness invites requests for research grants in 1959. Funds are available for projects that may contribute to basic understanding of eye function and pathology, or that may improve methods of diagnosis, treatment, or prevention of blinding eye disease. Grants will be made this spring for requests received prior to May 1, and inquiries may be addressed to Research Committee, National Society for the Prevention of Blindness, 1790 Broadway, New York 19.

Symposium on the Malabsorption Syndrome.—The National Vitamin Foundation will present a symposium on Absorption Mechanisms and the Malabsorption Syndrome March 3 at the Sheraton–East Hotel, New York City. The two sessions "Absorption Mechanisms" and "The Malabsorption Syndrome in Man," will have Drs. D. Mark Hegsted, Boston, and David Adlersberg, New York City, as chairman. A panel discussion will be conducted at 3:30 p. m. Dr. Norman Jolliffe, Director of the Bureau of Nutrition, Department of Health of the

City of New York, will speak on "The Anti-Coronary Club" at the dinner 7:30 p. m. For information write the National Vitamin Foundation, 149 East 78th St., New York 21, N. Y.

Caribbean Medical Cruise.—A 12½-day scientific program cruise, sponsored by the New York State Academy of General Practice, is planned for Oct. 22 to Nov. 4 on the M. S. Kungsholm of the Swedish American Line. There will be stop-overs at St. John and St. Thomas in the Virgin Islands; San Juan, Puerto Rico; Cap Hitien, Haiti; Havana, Cuba. A deposit of $50 will hold a reservation on any stateroom until April 1 at which time a deposit of 25% of the passage money will be required. The balance must be paid by Sept. 1. Prices will range from $330 and up depending on the location of the stateroom. Cruise membership will be limited to 425 persons. For information write Dr. Seymour Fiske, chairman of the cruise committee, 150 East 71 St., New York 21.

Request Residency Posts for Indian Physicians.—The Indian Medical Association requests offers from recognized hospitals for residency posts in all specialties for doctors from India—men and women—specially selected for graduate training in U. S. hospitals for the session commencing July 1. These doctors will have a good command of English, spoken and written. The hospitals must be approved by the U. S. State Department for Exchange-Visitor Program. This request of the Indian Medical Association has the approval of the American Medical Association. Interested hospitals are requested to communicate direct, by air mail, to the Honorary Secretary, Indian Medical Association, "Hanging Bridge," Daryaganj, Delhi-7, India, giving offers of posts, terms of appointment, etc., including maintenance, stipend, and the allotted number for Exchange-Visitor Program.

Meeting on Nuclear Medicine.—The sixth annual meeting of The Society of Nuclear Medicine will be held at the Palmer House, Chicago, June 18-20. Members of the society and guests desirous of participating in the scientific program should submit titles and abstracts, of no more than 250 words, to Dr. Donald W. Petit, Program Chairman, University of Southern California, School of Medicine, 1200 N. State St., Los Angeles 33, no later than March 1. Members and guests who wish to prepare a scientific exhibit should prepare a report of about 500 words explaining the purpose of the scientific exhibit as well as a brief description of the exhibit layout. Exact dimensions and other pertinent details should be forwarded to Dr. Murray E. Volk, Chairman, Committee on Scientific Exhibits, 5412 N. Clark, Chicago, together with the report.

Establish Fred L. Soper Lectures.—The Pan American Sanitary Bureau staff honored its director of 12 years on his retirement Feb. 1 with the establishment of the Fred L. Soper Lectures in International Health. The series will include five lectures to be given by outstanding medical personalities on successive years at leading schools of Public Health in the United States, Brazil, Chile, Mexico, and Canada. The first lecture will be given this fall by Dr. Soper himself at Johns Hopkins University's School of Hygiene, Baltimore. Bureau staff members will finance the lectures by voluntary donations to a special fund. Lecturers will be chosen by the host university and a committee of the PASB staff. Object of the series is "to bring Public Health students throughout the Americas into contact with scientific health authorities as outstanding as Dr. Soper."

Physicians in Congress.—Physician members of the 86th Congress number four, one less than the last Congress. November elections bring back Drs. Walter Judd, of Minnesota, Thomas Morgan and Ivor Fenton, both of Pennsylvania, and Dr. Thomas Alford, of Arkansas. Defeated at the polls were Drs. Will Neal, of West Virginia, and A. L. Miller, of Nebraska. Dr. Neal has been active on the health subcommittee of the House Interstate Committee and Dr. Miller on District of Columbia and Interior and Insular Affairs committees. Dr. Alford, a board opthalmologist of Little Rock, ran for public office for the first time. He has been practicing in Little Rock since 1948. Dr. Morgan is scheduled to take over the chairmanship of the House Foreign Affairs Committee on which Dr. Judd also serves. Dr. Morgan would become the first physician to head that committee in its 136 years.

Annual Meeting of Laryngologists.—The 80th annual meeting of the American Laryngological Association will be held March 8-9 at the Homestead, Hot Springs, Va. Dr. Fred W. Dixon, Cleveland, president of the association, will open the meeting. The following will be presented by invited speakers:

Carcinoma of the Nasopharynx, An Analysis of Thirty-Three Cases, Dr. L. Q. Pang, Honolulu, Hawaii.
Diagnosis of Chronic Inflammatory Lesions of the Sphenoid, Drs. James H. Maxwell and B. Jay Hill, Ann Arbor, Mich.
Cystic Fibrositis of the Pancreas and Nasal Mucosa, Dr. Moses Lurie, Boston.
A Histo-Chemical Study of the Pathogenesis of Nasal Polyps, Dr. Alexander Weisskopf, San Mateo, Calif.
Wegener's Granuloma, Drs. Joseph P. Atkins and Sylvan Eisman, Philadelphia.

Discussions will follow each presentation. The annual dinner will be held the evening of March 8. For information write Dr. James H. Maxwell, Out-Patient Bldg., University Hospital, Ann Arbor, Mich., Secretary.

Student Fellowships in Allergy.—The Scientific and Educational Council of the Allergy Foundation of America has announced the availability of a limited number of quarterly or summer scholarships at $500 each in approved medical schools in the United States and Canada. These scholarships are available to students who have creditably completed their second or third year in medical school, and are to be for a minimum of eight weeks of training in clinical and research allergy. Each medical school has been invited to submit the name of one applicant through the dean's office with a letter from the dean in support of the candidate's application, outlining the candidate's medical school record, the proposed research project, and under whose sponsorship it will be carried out. Direct applications from students will not be considered. All applications must be filed no later than March 1 and should be sent to Dr. Robert A. Cooke, chairman, Scientific & Educational Council, Allergy Foundation of America, 801 Second Avenue, New York 17.

Congress of Surgeons in Miami Beach.—The Southeastern Surgical Congress will hold its 27th annual assembly March 9-12 at the Deauville Hotel, Miami Beach. The presidential address will be given by Dr. Murray M. Copeland, Washington, D. C., director, department of oncology, Georgetown University Medical Center. The following will be presented by guest speakers:

Dissemination of Cancer and Its Prevention, Dr. Warren H. Cole, Chicago.
Management of Adrenal Hyperfunction, Dr. Olaf H. Pearson, New York City.
Advantage of Supervoltage X-ray Techniques to Surgeons in Diagnostic Radiology, Dr. Eugene P. Pendergrass, Philadelphia.
The Relationship Between Breast Cancer and Benign Breast Disease, Dr. Edward F. Lewison, Baltimore.
An Evaluation of Hemipelvectomy, Dr. Mark M. Ravitch, Baltimore.
Advances Made in Cancer Research, Dr. J. R. Heller, Bethesda, Md.
Bone Tumors, Dr. Charles F. Geschickter, Washington, D. C.
Plastic Surgical Principles in Farm, Industrial and Traffic Accidents, Dr. J. Barrett Brown, St. Louis.

Three panel discussions are planned: "Treatment of Advanced Cancer of the Breast," "Gynecology," and "Trauma." For information write Dr. B. T. Beasley, Secretary-Director General, The Southeastern Surgical Congress, 1032 Hurt Building, Atlanta 3, Ga.

Fellowship for Study on Pituitary Irradiation.—Donner Laboratory at the University of California, Berkeley, has announced the offering of a fellowship or training opportunity in connection with its pituitary irradiation studies. This program utilizes a high-energy particle beam for the study and investigation of the effects of pituitary irradiation on various conditions, including metastatic breast carcinoma, advanced diabetes mellitus with retinopathy, acromegaly, and pituitary tumors. Activities of the fellow will include participation in the irradiation program, in-patient and out-patient care, and extensive metabolic-endocrinological studies. Included will be training in the use of isotopes in research, investigation, diagnosis, and therapy. The fellowship will commence July 1, for one year, with the possibility of extension for an additional year. Interested physicians with residency training in metabolism-endocrinology, radiology, or hematology should write to Dr. John H. Lawrence, Director, Donner Laboratory, University of California, Berkeley 4, Calif. Inquiries should be accompanied by a complete curriculum vitae.

Surgeons Hold Sectional Meeting in St. Louis.—A comprehensive sectional meeting of the American College of Surgeons will be held in St. Louis, March 9-12. Headquarters will be the Kiel Auditorium, with many sessions scheduled also in St. Louis hospitals. The program will include hospital clinics, panel discussions, symposiums, scientific papers, technical exhibits, medical motion pictures, and cine clinics in general surgery and in the specialties of thoracic surgery, urology, gynecology and obstetrics, ophthalmic surgery, and orthopedic surgery. Dr. Frank McDowell, St. Louis, associate clinical professor of surgery, Washington University School of Medicine, is chairman of the local advisory committee on arrangements for the scientific program. The joint nurses program, now an annual feature of this four-day meeting, will include discussions on comprehensive care of the patient who has successfully undergone pelvic evisceration, open technique in the management of burns, congenital heart disease, and other problems. Tours and demonstrations will be held at Barnes Hospital, Cardinal Glennon Children's Hospital, Central Institute for the Deaf, Cochran Veterans Hospital, Firmin Desloge Hospital, Jewish Hospital, Missouri School for the Blind, St. Anthony's Hospital (Poliomyelitis Center), St. Louis Children's Hospital, St. Louis City Hospital, St. Luke's Hospital, and Shriners' Hospital for Crippled Children. Dr. H. Prather Saunders, associate director, American College of Surgeons, is in charge of the sectional meeting program for the college.

FOREIGN

Symposium on Toxic Substances in Prague.—The International Symposium on Maximum Allowable Concentrations of Toxic Substances in Industry will be held at Prague, April 14-17. The symposium will be arranged under the aegis of the Permanent Committee and International Association on Occupational Health and the International Union of Pure and Applied Chemistry. The following subjects will be treated:

1. The investigation of present-time definitions and conceptions of maximum allowable concentrations in different countries.
2. The evaluation of present-time methods and procedures used in different countries for the determination and fixing of maximum allowable concentrations.
3. Maximum allowable concentrations in biological materials.
4. The evaluation of the importance of suitable methods of chemical analyses, physical methods and methods of sampling used in industry.
5. General discussion.

President of the Organizing Committee is Prof. Rene Truhaut, Paris, and General Secretary is Prof. Jar. Teisinger, Prague II., Karlovo n.33 (Czechoslovakia).

CORRECTION

Dr. Rosenbaum at Washington University.—In the article by Dr. Eva F. Dodge et al. on "Late Sequelae of Saddle Block Anesthesia in Obstetrics" in THE JOURNAL, Jan. 31, 1959, page 430, second column, fourth line in the second paragraph, the authors stated that "Rosenbaum and co-workers at St. Louis University, in 1952, reported 6 cases. . . ." Dr. Rosenbaum writes that he and his co-workers were all affiliated with Washington University and not St. Louis University.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: *Oral.* Phoenix, April 5-10. All applications already on file. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

AMERICAN BOARD OF DERMATOLOGY: *Written.* Several Cities, Oct. 5. *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications is July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

AMERICAN BOARD OF INTERNAL MEDICINE: *1959 Schedule—Written,* Oct. 19. Final date for filing application is May 1. *Oral.* For candidates in the Midwest. Chicago, April 15-18. Final date for filing application was Jan. 1. *Oral.* For candidates on the West Coast. Final date for filing application is March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application is March 1. *Examination in the Subspecialties. Gastroenterology.* Philadelphia, April 17-18. Final date for filing application was Feb. 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *I. Oral and Clinical.* Chicago, May 8-19. Formal notice of the exact time of each candidate's examination will be sent him in advance of the examination dates. Candidates who participated in the Part I examinations will be notified of their eligibility for the Part II examinations as soon as possible. Deadline for receipt of new and reopened application for the 1960 examinations is Aug. 1, 1959. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* (Part II) Philadelphia, June 2-6; St. Louis, Oct. 6-10. Written (Part I), Jan. 25, 1960. Application for 1960 must be filed before July 1, 1959. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part I.* Washington, D. C., Denver, Colorado and Rochester, Minn., Mar. 26-27. Deadline for filing application was Nov. 30. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* Chicago, Oct. 5-9. Final date for filing application is February. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PATHOLOGY: Boston, April 16-19. Final date for filing application is Feb. 28. Sec., Dr. Edward B. Smith, 1100 W. Michigan St., Indianapolis 7.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION: *Written, Part I,* and *Oral, Part II.* Philadelphia, June 12-13. Final date for filing application is February 15. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral and Written.* Miami, Fla., Oct. 15-17. Final date for submitting case reports is July 1. Corresponding Secretary, Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

AMERICAN BOARD OF PREVENTIVE MEDICINE: *Written. Public Health.* Regional, Apr. 9-11. *Occupational Medicine.* Chicago, Apr. 17-19. *Aviation Medicine.* Los Angeles, Apr. 24-26. Final date for filing application for all three examinations is Jan. 15. Sec., Dr. Tom F. Whayne, 3438 Walnut St., Philadelphia 4.

AMERICAN BOARD OF PROCTOLOGY: *Oral and Written.* Philadelphia, September. Final date for filing application is March. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New Orleans, Mar. 16-17; Chicago, Oct. 19-20; New York, Dec. 14-15. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Special Examination.* Cincinnati, Mar. 16-19, 1959. Final date for filing application was Nov. 1. *Examination.* Chicago, June 2-4. If needed a special examination will be offered at this time in Nuclear Medicine to diplomates in Radiology or Therapeutic Radiology. The deadline for filing applications is April 1. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written* examinations (Part I) will be held on December 2, 1959 at various centers to be announced later. Candidates are urged to apply several months before completion of training requirements although the closing date for filing applications is August 1. Those completing training requirements after September 30 cannot be considered for the Part I examination in December of the same year. *Part II.* Durham, No. Car., March 9-10; San Francisco, April 13-14; Indianapolis, May 11-12; Columbus, Ohio, May 14-15. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

BOARD OF THORACIC SURGERY: *Oral.* Los Angeles, September. Final date for filing application is July 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2.

AMERICAN BOARD OF UROLOGY: The oral will be given in Chicago in February 1959. Sec., Dr. William Niles Wishard, Jr., 30 Westwood Road, Minneapolis 26.

GOVERNMENT SERVICES

NAVY

Medical Military Training.—A two-week course in Medical Military Training beginning March 9, 1959, will convene at the Naval Medical School, National Naval Medical Center, Bethesda, Md. The first week will be devoted to medical aspects of special weapons and radioactive isotopes with particular reference to personnel casualties from atomic explosions. The second week will be devoted to professional topics of concern to military medicine, including discussions on reserve medical programs of the Armed Forces. As this course has new subjects, new material, and has been revised to bring it up to date, it is highly recommended for officers to repeat this training in the event they have participated in previous classes. Naval Reserve Medical Department Officer personnel from the First, Third, Fourth, Sixth, Eighth, and Ninth Naval Districts may attend on a limited quota basis. No security clearance is required.

VETERANS ADMINISTRATION

Vocational Rehabilitation.—In order to facilitate the rehabilitation of disabled veterans, they are now allowed to begin vocational training while they still are patients in VA hospitals. They must, however, be far enough along in their hospital treatment to be able to leave the hospital part of the day to attend school or a training establishment. Another new feature permits veterans to start vocational rehabilitation training even if they cannot be expected to complete it by the termination date for such training as established by law. In such cases, however, arrangements must be made for some agency other than the VA—such as a State Rehabilitation Agency—to pick up where the VA has to leave off. The termination date for disabled veterans of the Korean conflict who left the service before Aug. 20, 1954, is Aug. 20, 1963. The date for those who left the service after Aug. 20, 1954, is nine years from separation or Jan. 31, 1964, whichever comes first. In some instances, these dates can be extended. Only a few World War II disabled still are eligible for vocational rehabilitation, and their termination date is July 25, 1960. A third new feature permits the VA to give placement assistance as well as personal counseling to disabled veterans after they have completed their vocational training if needed. Previously, VA counseling was given only before a veteran started his training or while he was in training.

PUBLIC HEALTH SERVICE

Regular Corps Examinations for Medical Officers.—A competitive examination for appointment of medical officers to the Regular Corps of the United States Public Health Service will be held in various places throughout the country on April 21, 22, 23, and 24, 1959. Appointments provide opportunities for career service in clinical medicine, research, and public health. They will be made in the ranks of assistant and senior assistant surgeons, equivalent to Navy ranks of lieutenant (j. g.) and lieutenant respectively. Entrance pay for assistant and senior assistant surgeons with dependents is $7,470 (assistant grade applicants are assigned the temporary grade of senior assistant). Provisions are made for promotions at regular intervals.

Benefits include periodic pay increases, 30 days annual leave, sick leave, medical care, retirement for age or disability, retirement pay which is 75% of annual basic pay at time of retirement, and other privileges. Active duty as a Public Health Service officer fulfills the obligation of Selective Service. Requirements are United States citizenship, age of at least 21 years, and graduation from a recognized school of medicine. For the rank of assistant surgeon and for senior assistant surgeon at least 7 and 10 years, respectively, of collegiate and professional training and appropriate experience is needed. Entrance examinations will include an oral interview, physical examination, and comprehensive objective examinations in the professional field. Application forms may be obtained by writing to the Surgeon General, Public Health Service (P), Washington 25, D. C. Completed application forms must be received in the Division of Personnel no later than March 6, 1959.

Influenza Epidemic.—Surgeon General Burney of the Public Health Service alerted state and territorial health officers to the increase in reports of outbreaks of various types of influenza in several European countries. Although no outbreak in the United States has been reported, the disease may be introduced into this country by persons entering or returning from Europe. Health officers are urged to report promptly any laboratory confirmed cases. The British press on Feb. 6 stated that a wave of influenza was swamping the hospitals in England. Type A influenza is also reported to affect large numbers of persons in the U. S. S. R. Type B has been identified in Italy and the Netherlands. Practicing physicians are urged to vaccinate such groups as the aged, the chronically ill, pregnant women, hospital staff personnel, and others whose incapacitation by illness would disrupt essential services.

DEATHS

Albee, George Cummings, Berkeley, Calif.; Medical Department of the University of California, San Francisco, 1905; veteran of World War I; died in the Herrick Memorial Hospital Dec. 5, aged 81.

Aldrich, Hattie Bassett, Caney, Kan.; Kansas Medical College, Medical Department of Washburn College, Topeka, 1904; died Dec. 8, aged 89.

Allen, Daisy Emery Ⓜ Fort Worth, Texas; Fort Worth School of Medicine, Medical Department of Fort Worth University, 1897; at one time professor of pediatrics at the Dallas Medical College; died Dec. 7, aged 82.

Allen, Duff Shederic, St. Louis; Washington University School of Medicine, St. Louis, 1919; formerly on the faculty of his alma mater; member of founders group of the American Board of Surgery; appointed a member of the state board of medical examiners in 1953 and later became chairman; member of the Missouri State Medical Association, Society of University Surgeons, and the American Association for Thoracic Surgery; associated with St. Louis Children's and St. Louis Maternity hospitals; served as associate editor of *Journal of Thoracic Surgery;* died in St. John's Hospital Dec. 7, aged 63.

Aron, Hans Carl Siegfried Ⓜ Chicago; Friedrich–Wilhelms–Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1908; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; served on the faculty of Northwestern University Medical School; at one time on the faculty of the University of the Philippines College of Medicine in Manila; associated with the Children's Memorial Hospital; died Dec. 11, aged 77.

Bishop, Henry Hawkins, State Sanatorium, Ark.; Kentucky University Medical Department, Louisville, 1905; veteran of World War I; associated with the Arkansas Tuberculosis Sanatorium; died in Little Rock Dec. 8, aged 76.

Blain, Alexander William Ⓜ Detroit; born in Detroit March 4, 1885; Detroit College of Medicine, 1906; formerly on the faculty of his alma mater, now known as the Wayne University College of Medicine; past-president of the Wayne County Medical Society, Detroit Academy of Surgery, and the Alumni Association of Wayne University; member of the board of the Michigan Horticultural Society, serving as president in 1944-1945; a trustee of the Detroit Zoological Society; fellow of the Royal Society of Arts, New York Academy of Sciences, American College of Surgeons and served as a member of its board of governors, and the American Association for the Advancement of Science; member of the public welfare commission of Detroit from 1926 to 1933 and president 1931-1932; member and past-president of the Superintendents of the Poor of Wayne County; member of the commission of conservation for the state of Michigan from 1939 to 1945; past-president of the Michigan Audubon Society; member of the Nu Sigma Nu, Sigma Xi, and Alpha Omega Alpha; director of the Gorgas Memorial Institute; chief of staff, Blain Clinic; senior surgeon at Alexander Blain Hospital; consulting surgeon at the Wayne County General Hospital, Eloise, Detroit Memorial Hospital, and the Receiving Hospital of the City of Detroit; on the consulting staff of Detroit Tuberculosis Sanitarium; specialist certified by the American Board of Surgery; member of the editorial staff, Washington Institute of Medicine, Washington, D. C., and member of the editorial board, *Revista Argentina–Norteamericana de Ciencias Medicas;* in 1930 was presented with an honorary master of science degree by his alma mater; died in the Alexander Blain Hospital Dec. 14, aged 73.

Blandford, William Clarke Ⓜ Atlanta, Ga.; Emory University School of Medicine, Atlanta, 1917; died Dec. 1, aged 71.

Blanton, Howson Wallace Ⓜ Richmond, Va.; Columbia University College of Physicians and Surgeons, New York City, 1917; associate professor of clinical medicine at the Medical College of Virginia; veteran of World War I; past-president of the Hampden Sydney Alumni Association; died in St. Luke's Hospital Dec. 12, aged 66.

Brenza, Sylvester A., Deerfield, Ill.; Chicago College of Medicine and Surgery, 1910; associated with Holy Cross, Englewood, and St. Mary's hospitals in Chicago, where he was president of the Metropolitan State Bank; died in Gulfport, Miss., Dec. 5, aged 67.

Brown, Hugh Osborne Ⓜ Salt Lake City, Utah; Northwestern University Medical School, Chicago, 1937; specialist certified by the American Board of Anesthesiology; member of the American Society of Anesthesiologists, Inc., of which he was vice-president in 1943; on the faculty of the University of Utah College of Medicine; served as a fellow in anesthesiology at the Mayo Foundation in Roches-

Ⓜ Indicates Member of the American Medical Association.

ter, Minn.; formerly on the staff of the Cook County Hospital in Chicago; chief of anesthesia at St. Mark's Hospital, where he died Dec. 5, aged 48.

Bryan, Herman Lawrence, Dallas, Texas; University of Texas School of Medicine, Galveston, 1952; on the faculty of the University of Texas Southwestern Medical School; veteran of World War II; interned at the Jackson Memorial Hospital in Miami, Fla.; served as resident at the Charity Hospital of Louisiana in New Orleans and the Parkland Memorial Hospital; died Dec. 2, aged 36.

Bush, Charles R., Macon, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1894; died Dec. 5, aged 86.

Collier, Henry L., Norfolk, Va.; University College of Medicine, Richmond, 1909; for many years a director of the Daily Press, Inc., and vice-president of the Peninsula Newspaper Publishing Corporation; a director of the Hampton Roads Broadcasting Corporation (WGH); served on the staffs of Norfolk General Hospital, De Paul Hospital, and Leigh Memorial Hospital; died Dec. 4, aged 72.

Cook, Benjamin Biscombe, Fern Glen, Pa.; Medico-Chirurgical College of Philadelphia, 1913; died Dec. 6, aged 69.

Cushing, Russell George Ⓜ Detroit; Detroit College of Medicine and Surgery, 1929; member of the American Academy of General Practice; on the staff of the Holy Cross Hospital; died Dec. 1, aged 56.

Davis, Urey Guess, St. Petersburg, Fla.; Louisville (Ky.) Medical College, 1907; veteran of World War I; at one time practiced in Russellville, Ky., where he was health officer of Logan County; for many years associated with various Veterans Administration hospitals; died in the Veterans Administration Hospital in Bay Pines Dec. 9, aged 73.

DeVelling, John Robin Ⓜ Jackson, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1912; fellow of the American College of Surgeons; veteran of World War I; served in the regular U. S. Army; at one time practiced in Rosiclare, Ill., and Laurel, Miss.; died in the University Hospital Dec. 2, aged 72.

Dooley, Marion Sylvester Ⓜ Syracuse, N. Y.; Syracuse University College of Medicine, 1914; professor emeritus of pharmacology at State University of New York College of Medicine; past-honorary-president of the International Anesthesia Research Society; served as a member of the U. S. Pharmacopoeia Revision Committee many years; editor of "Interns Handbook"; joint author of "Pharmacology and Therapeutics in Nursing"; on the honorary staff of the Hospital of the Good Shepherd, where he died Dec. 13, aged 78.

Dudley, Stowell Barnard Ⓜ Caldwell, Idaho; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1897; veteran of World War I; died in Parma Dec. 2, aged 92.

Edwards, Charles John Jr., Natchez, Miss.; Tulane University School of Medicine, New Orleans, 1940; veteran of World War II; died in New Orleans Dec. 16, aged 46.

Eller, William Douglas Ⓜ New York City; born in New York City May 12, 1910; University of Arkansas School of Medicine, Little Rock, 1941; specialist certified by the American Board of Dermatology and Syphilology; fellow of the New York Academy of Medicine; member of the American Academy of Dermatology and Syphilology and the Association of Military Surgeons of United States; a trustee of the Pan-American Medical Association and vice-president of its dermatological section; veteran of World War II; clinical instructor of dermatology and syphilology, New York University College of Medicine; on the staffs of the New York University–Bellevue Medical Center and Metropolitan Hospital; wrote many articles on his specialty, and was co-author of "Tumors of the Skin: Benign and Malignant"; died in the Midtown Hospital Dec. 9, aged 48.

Emrich, William Ⓜ Hebron, Md.; University of Maryland School of Medicine, Baltimore, 1902; died in the Peninsula General Hospital in Salisbury Dec. 15, aged 79.

Farmer, David Kyser Ⓜ Mansfield, Ill.; University of Louisville (Ky.) School of Medicine, 1935; served overseas during World War II; health officer of Mansfield; on the staff of the Burnham City Hospital in Champaign; died Dec. 15, aged 49.

Foreman, Harry Lee Ⓜ Indianapolis; Indiana University School of Medicine, Indianapolis, 1917; past-president of the Indianapolis Medical Society; member of the American Academy of General Practice; served as superintendent of the Indianapolis City Hospital; associated with Methodist and St. Vincent's hospitals; died Dec. 3, aged 75.

Frazer, George Brasfield, Houston, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1902; died Dec. 3, aged 79.

Gettings, Joseph Roland, Buffalo; University of Buffalo School of Medicine, 1925; served on the faculty of his alma mater; associated with the Emergency Hospital and Sisters of Charity Hospital; died Dec. 15, aged 58.

Mayers, Morton Myron Ⓜ Los Angeles; University of California School of Medicine, San Francisco, 1930; assistant clinical professor of surgery at the University of California School of Medicine; specialist certified by the American Board of Urology;

member of the American Urological Association; fellow of the International College of Surgeons and the American College of Surgeons; veteran of World War II; associated with the Queen of Angels Hospital, where he died Nov. 20, aged 54.

Mellies, Edward, Owensville, Mo.; Homeopathic Medical College of Missouri, St. Louis, 1893; member of the school board; died in St. Francis Hospital, Washington, Oct. 31, aged 87.

Mitchell, Charles Otis, Fresno, Calif.; University of Colorado School of Medicine, Denver, 1907; an associate member of the American Medical Association; past-president and secretary of the Fresno County Medical Society; served in France during World War I; died Nov. 23, aged 80.

Moore, Cannon Deuger Ⓜ Oklahoma City, Okla.; Baylor University College of Medicine, Dallas, Texas, 1922; associated with the Wesley Hospital; died in the Mercy Hospital Nov. 12, aged 61.

Motel, William Goodrich Ⓜ Chicago; University of Illinois College of Medicine, Chicago, 1937; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; veteran of World War II; associated with South Shore Hospital, Jackson Park Hospital, and the Michael Reese Hospital, where he died Dec. 9, aged 46.

O'Hara, Thomas Aloysius, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1897; for many years on the staffs of St. Agnes Hospital and the Hospital of the University of Pennsylvania; died Nov. 18, aged 84.

Parker, Paul Martin, Moravia, N. Y.; New York Homeopathic Medical College and Flower Hospital, New York City, 1915; veteran of World War I; formerly county coroner; died in Clifton Springs, Nov. 30, aged 74.

Pollock, Clifford J. Ⓜ Holland, Ohio; Toledo Medical College, 1912; died in the Mercy Hospital, Toledo, Nov. 30, aged 74.

Reed, Hugh Stephen Ⓜ Guide Rock, Neb.; Keokuk (Iowa) Medical College, College of Physicians and Surgeons, 1906; died in St. Joseph's Hospital, Concordia, Nov. 16, aged 79.

Renfrew, Francis Charles, Portland, Ore.; Miami Medical College, Cincinnati, 1903; at one time practiced in Long Beach, Calif., where he was associated with the Community Hospital, and served as president of the Chamber of Commerce; died Nov. 29, aged 82.

Renken, Paul William Ⓜ New Orleans; Tulane University School of Medicine, New Orleans, 1931; on the faculty of his alma mater; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology; president of the New Orleans Academy of Ophthalmology; associated with the Charity and Southern Baptist hospitals; veteran of World War II; died Nov. 22, aged 51.

Rhodes, Walter R. Ⓜ Toledo, Ill.; Rush Medical College, Chicago, 1902; associated with St. Anthony Memorial Hospital in Effingham and the Memorial Hospital in Mattoon; died Nov. 29, aged 80.

Richards, George Girard, Pinconning, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1904; died Nov. 14, aged 81.

Robinson, Wilton Howarth Ⓜ Pittsburgh; Western Pennsylvania Medical College, Pittsburgh, 1900; died in the Southside Hospital Nov. 20, aged 80.

Runyon, Leon Iral Ⓜ Obion, Tenn.; University of Tennessee College of Medicine, Memphis, 1942; veteran of World War II; on the staff of the Obion County General Hospital in Union City; died Nov. 9, aged 49.

Russell, Paul Livingston Ⓜ Inglewood, Calif.; University of Minnesota Medical School, Minneapolis, 1944; member of the American Academy of General Practice; veteran of World War II; associated with Hawthorne (Calif.) Community Hospital, Centinela Valley Community Hospital and Daniel Freeman Memorial Hospital; died Nov. 17, aged 42.

Ryan, William John Joseph, San Diego, Calif.; Northwestern University Medical School, Chicago, 1922; veteran of World War II; died Nov. 1, aged 64.

Smith, Prentiss Edward Ⓜ Hattiesburg, Miss.; Tulane University School of Medicine, New Orleans, 1926; member of the Southeastern Surgical Congress; fellow of the International College of Surgeons and the American College of Surgeons; associated with the Forrest County General Hospital and the Methodist Hospital, where he died Nov. 30, aged 57.

Steinbach, Henry Barthell Ⓜ Detroit; State University of Iowa College of Medicine, Iowa City, 1920; member of the American College of Cardiology and the American College of Gastroenterology; fellow of the American College of Physicians; veteran of World War I; associated with the Grace Hospital, Harper Hospital, and the Woman's Hospital; died in New York City Nov. 21, aged 65.

Strachan, Harry Morris Ⓜ Shaker Heights, Ohio; University of Louisville (Ky.) Medical Department, 1911; specialist certified by the American Board of Preventive Medicine; member of the Aero Medical Association; veteran of World War I; served as examiner for the Civil Aeronautics Administration; died Nov. 18, aged 71.

Taliaferro, Robert Milton Ⓜ Lynchburg, Va.; Medical College of Virginia, Richmond, 1897; for many years surgeon for the Norfolk and Western Railway and physician for Lynchburg Jail; died in Staunton Nov. 26, aged 84.

Tennant, Charles C., Farmville, Va.; University of Virginia Department of Medicine, Charlottesville, 1904; veteran of World War I; died in Charlottesville Dec. 1, aged 80.

Thompson, Holman Bennett Ⓜ Fort Smith, Ark.; University of Arkansas School of Medicine, Little Rock, 1915; died Nov. 24, aged 72.

Trent, Russell John, Lieut. Commander, U. S. Navy, retired, La Jolla, Calif.; University and Bellevue Hospital Medical College, New York City, 1914; veteran of World Wars I and II; retired June 30, 1937; died Nov. 5, aged 66.

Vacin, Milo Edward Ⓜ Riverside, Ill.; University of Illinois College of Medicine, Chicago, 1929; veteran of World War II; dean and treasurer of the Worsham College of Mortuary Science; vice-president and past-president of the staff, Bethany Sanitarium and Hospital, Chicago, where he died Nov. 22, aged 57.

Van de Sand, Gerard F. Ⓜ Fulton, Ill.; Chicago College of Medicine and Surgery, 1916; served as examining physician for the draft board in World War II; for many years was the city health officer; died Nov. 5, aged 77.

Van Loan, James Casper Plimpton, Keene, N. Y.; College of Physicians and Surgeons, medical department of Columbia College, New York City, 1891; for many years practiced in New York City; died in the Keene Valley (N. Y.) Hospital Nov. 14, aged 90.

Villien, Joseph A., Maurice, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1890; served as mayor, postmaster, and on the Vermilion parish school board; a director of the Abbeville and Trust Company; died in Abbeville Nov. 5, aged 88.

Vitols, Theodore Mikelis Ⓜ Minneapolis; Latvijas Universitäte Medicinas Fakultate, Riga, Latvia, 1928; died in Toronto, Ont., Canada, Nov. 3, aged 55.

Vye, Theodore Roland Ⓜ Billings, Mont.; College of Medical Evangelists, Loma Linda and Los Angeles, 1928; fellow of the International College of Surgeons and the American College of Surgeons; secretary-treasurer of the Montana Medical Association; president of the Montana Physicians' Service; associated with St. Vincent Hospital and the Billings Deaconess Hospital; died Nov. 30, aged 56.

Wainright, Melvin A. Rice Ⓜ Shrewsbury, N. J.; Temple University School of Medicine, Philadelphia, 1938; veteran of World War II; chief of staff and president of the medical board, Riverview Hospital in Red Bank; died in Red Bank Nov. 3, aged 46.

Walker, Howard McKinley Ⓜ Dodgeville, Wis.; Rush Medical College, Chicago, 1927; clerk of the school board of Dodgeville; city health officer; died in the Dodgeville General Hospital Nov. 21, aged 57.

Walker, Samuel G., Hot Springs National Park, Ark.; Meharry Medical College, Nashville, Tenn., 1908; died Nov. 3, aged 74.

Wanner, Jay George Ⓜ Rock Springs, Wyo.; Chicago Medical School, 1918; veteran of World War II; at one time district surgeon for the Union Pacific Railroad in Green River; served as president of the Sweetwater County Medical Society; associated with Memorial Hospital of Sweetwater County; died Nov. 27, aged 63.

Warfield, William Pollock Ⓜ Clarksdale, Miss.; University of Tennessee College of Medicine, Memphis, 1932; member of the American Academy of General Practice; died Nov. 30, aged 52.

Watkins, McLeod McInnis, Cincinnati; Vanderbilt University School of Medicine, Nashville, Tenn., 1958; intern, Cincinnati General Hospital; died Nov. 4, aged 24.

Weiss, Joseph Guy, Pontiac, Mich.; Wayne University College of Medicine, Detroit, 1935; during World War II associated with the U. S. Public Health Service Reserve; member of the American Academy of General Practice; resident in psychiatry at the Pontiac State Hospital; died Nov. 6, aged 51.

Worth, Archibald Carter Jr., Albany, N. Y.; New York Homeopathic Medical College and Flower Hospital, New York City, 1910; member of the Medical Society of the State of New York; died in the Memorial Hospital Nov. 29, aged 73.

Yarbrough, Silas McWilliams Ⓜ Gainesville, Texas; Vanderbilt University School of Medicine, Nashville, Tenn., 1923; veteran of World War I; past-president of the Cooke County Medical Society; past-president of the Gainesville Kiwanis Club; died Nov. 9, aged 59.

Yarling, John E. Ⓜ Peru, Ind.; Medical College of Ohio, Cincinnati, 1897; past-president and secretary of the Miami County Medical Society; served as mayor, city health officer, county health officer, and county coroner; at one time member of the city council; president of the First Federal Savings and Loan Association; honorary staff member, Dukes–Miami County Hospital, where he died Nov. 8, aged 89.

FOREIGN LETTERS

BRAZIL

Hypothermia and Circulatory Arrest.—Dr. G. M. Santos and co-workers of the Santa Theresa Hospital, Rio de Janeiro, (*Revista brasil. cir.* **36**:279, 1958) anesthetized 25 dogs with pentothal (Thionembutal) sodium and curare (Flaxedyl) in varied doses, and subjected them to orotracheal intubation and controlled respiratory ventilation by means of an apparatus with either positive or positive and negative alternating pressures or a respiratory pouch. Hypothermia was produced by immersion in cold water for an average period of 30 minutes, which caused the rectal temperature to drop to 31 C (87.8 F). Each animal was removed from the bath, the thorax was opened, and circulatory arrest induced by ligature of the caval veins for an average period of eight minutes. After this they were sutured and warmed until the rectal temperature reached 36 C (96.8 F).

The authors observed that the decrease of the dog's rectal temperature during the cold bath was regular, and averaged 1 C (1.8 F) for each minute. The greater the body weight of the animal the slower was the fall of its rectal temperature. The velocity of the fall of temperature was increased by administration of curare. The fall of temperature (average 4 C [7.2 F]) persisted after the animals were removed from the bath. The frequency of the heartbeats diminished with the fall of temperature. The heart rate became stable when the minimal rectal temperature was attained (average 27 C [80.6 F]). The blood pressure also decreased, although there was a tendency, while in the cold bath, for it to increase about 10 mm. Hg after an initial fall of about 20 mm. Hg. Ventricular fibrillation was a frequent, serious, and unexpected accident during hypothermia. Doses of pentothal sodium above 15 mg. per kilogram of body weight and body temperatures below 26 C (78.8 F) were responsible for ventricular fibrillation. Coronary perfusion with neostigmin was useful in preventing fibrillation. Electric defibrillation and heart massage, effective in 15 of 16 cases, was the ideal treatment for ventricular fibrillation. The duration of hypothermia was considered important in evaluating the final results and postoperative physiological conditions. The best experimental conditions for a cardiac arrest of eight minutes are a rectal temperature around 26 C (78.8 F) and slight hypnosis induced by 1 mg. of curare per kilogram of body weight. For complete recovery the whole procedure should not exceed two hours.

Adenocarcinomatous Polyps of the Colon and Rectum.—The importance of the adenomas of the colon and the rectum as precursors of carcinoma has been gaining recognition. Dr. Sylvio Levy of the Hospital dos Servidores, Rio de Janeiro (*Hospital* **54**:483, 1958) reported a series of 6,604 successive patients in 102 (1.54%) of whom a diagnosis of polyps was made (98 with polyps of the rectum and 4 with polyps of the sigmoid colon). The ratio of males to females was 2:1. Of the 102 patients histological examinations were made on 67 with the following diagnoses: inflammatory polyps, 4; lobulated adenomas, 45; and carcinomas in adenomas, 18. One curious aspect of this series was the presence of polyps in three cases, all considered malignant, in patients in the first decade of life.

Diabetic Vascular Syndrome.—Dr. P. C. Rebocho and co-workers of the São Paulo State University (*Hospital* **54**:677, 1958) studied 50 patients with diabetes (average age 59.3 years). Retinopathy of various degrees was present in 46 and was markedly influenced by the state of control of the diabetes. Intercapillary glomerulosclerosis was present in 18 and 33 had signs of myocardial disease. Arterial hypertension was present in 34 among whom 24 were obese. The blood cholesterol level was determined in 20 and was increased in 13. Peripheral vascular lesions were found in 27. Obesity was present in 15 of these and an increased cholesterol level in 8. Peripheral vascular lesions did not depend on the state of control of the diabetes. Neuropathies were found in 40 but were not correlated with the state of control of the disease. Although the authors could not establish a relationship between the various types of lesion observed, their attention was attracted to the frequency of the simultaneous presence of several lesions. Seven patients showed two types of lesion, 16 had three, 13 had four, and 7 had five. These figures confirm the present theory that the vascular lesions of diabetes are localized manifestations of a generalized disease. Whether the arterial lesions are mere complications of arteriosclerosis or constitute a diabetic angiopathy is not yet known. The authors stress the necessity of looking for vascular lesions in every patient with diabetes.

The items in these letters are contributed by regular correspondents in the various foreign countries.

GERMANY

Isoniazid and Vitamin B_6 Metabolism.—A frequently observed side-effect from isoniazid used in the treatment of tuberculosis is polyneuritis. This is ascribed to the antimetabolic action of the drug on vitamin B_6 metabolism. Niacin metabolism is not disturbed. An antagonism between isoniazid and vitamin B_6 in growing micro-organisms has been reported several times. The derangement of vitamin B_6 functions during isoniazid therapy also affects tryptophan metabolism. Knapp and co-workers (*Klin. Wchnschr.* **36**:819, 1958) found that 9 of 17 patients with various forms of skin tuberculosis excreted more than 30 mg. of xanthic acid in the urine after administration of 10 Gm. of dl-tryptophan. In 322 patients with various forms of skin tuberculosis treated with 4 to 7 mg. of isoniazid per kilogram of body weight per day, such side-effects as giddiness, urticaria, gastrointestinal disorders, depression, paresthesias, and neuritides were observed in 123. The vitamin B_6 deficiency was undoubtedly due to the isoniazid. There was, however, evidence that the body could adapt itself to isoniazid. As a result of this adaptation, vitamin B_6 deficiency and also subjective symptoms decreased. The authors argue convincingly for a competitive antivitamin B_6 effect exerted by isoniazid. In tests with healthy subjects the antagonism was shown to exist at least for part of the vitamin B_6 functions. The results do not yet explain the mechanism of this antagonism.

Treatment of Pernicious Anemia.—A series of 39 patients with compensated and 22 with decompensated pernicious anemia was treated exclusively with various combinations of vitamin B_{12} and intrinsic factor given by mouth. The patients were given, every second day, 5 mcg. of vitamin B_{12} and the corresponding quantity of an intrinsic factor preparation. Of 17 patients, 11 became decompensated in the course of five years; i. e., their erythrocyte counts declined below 4,000,000 per cubic millimeter and their hemoglobin concentrations below 80%. Their feeling of well-being deteriorated, but there were no neurological complications.

Summarizing the results I. Boll (*Arztl. Wchnschr.* **13**:930, 1958) concluded that the favorable effect observed in the first two years of oral treatment was not maintained when the treatment continued for several years. Intramuscular injections of vitamin B_{12}, even in low dosage, proved superior to oral treatment. In 5 patients with decompensated anemia oral treatment failed to achieve compensation at any time, and of 13 patients who became compensated at some time during the initial period of treatment 8 became decompensated again within two years, a total of almost 80% unsatisfactory results. It may be that intrinsic factor from hog stomach is not sufficiently effective for prolonged treatment or an antibody reaction to the heterologous substrate may develop on continuing administration. In another study it was observed that patients receiving a single intramuscular dose of 1 mg. of vitamin B_{12} were compensated for longer than a year, notwithstanding reports that after administration of such a large dose more than 50% is excreted in the urine within a few days.

Epidemic of Erythema Infectiosum.—Since the middle of 1958 a violent epidemic of erythema infectiosum has been observed in West Germany. The epidemic occurred first in Schleswig-Holstein and Oldenburg, and then spread southward. A similar but not so violent epidemic was observed in 1866 in Graz and in the winter of 1913-1914 in Breslau. The epidemic was almost certainly caused by a virus. In the virological laboratories of the dermatological clinic of Hamburg University an organism was isolated and neutralized, and complement-fixing antibodies were detected in the patients' serums. Most probably it was a variant of an already known virus. The exanthem (circular, red, and maculopapular) usually started in the face and spread to the extremities and the trunk. Temperatures were seldom higher than 38 C (100.4 F) and, apart from the severe itching, the general health was hardly impaired. The incubation period was 7 to 14 days, and the communicability was small. Because of this and the mild course of the disease isolation was not considered necessary. The treatment was symptomatic: antihistaminics were given to soothe the itching, antipruritic embrocations applied, and vitamin C was given empirically.

Metabolism of Cancer Cells.—At the meeting of the German Association of Scientists and Physicians in Wiesbaden Professor Warburg stated that there is most probably no exception to the rule that normal body cells "breathe" while cancer cells do not breathe but ferment. Fermentation was the energy-supplying reaction of life when the atmosphere did not yet contain oxygen. As fermentation requires, for the production of the same quantity of energy, about 10 times as much substance as breathing, it is a less refined kind of biological energy production. In the course of phylogenesis, fermentation was supplanted by breathing (oxidation) in all the higher forms of life, but all living beings still possess the capacity to ferment if the cells are deprived of oxygen. Breathing is the attribute of normal growth, fermentation the attribute of abnormal growth. In the development of the cancer the following metabolic pattern is observed: at first abnormal growth, disengagement of respiration, and increase of fermentation. This is followed by a decrease of respiration. In the last phase of carcinogenesis the tumor cells develop a resistance to cytolysins and can then grow on, infiltrating and metastasizing. In water x-rays in the presence of

oxygen produce hydrogen peroxide. Cancer cells contain less catalase than normal cells and are thus extremely sensitive to hydrogen peroxide. The sensitivity to radiation of cancer cells should therefore increase if during radiation the erythrocytes, which contain an enormous quantity of catalase, could be eliminated. The radiated parts of the body would thus have to contain a liquid which is free from red blood cells but nevertheless contains oxygen.

Cystic Fibrosis.—Cystic fibrosis of the pancreas is characterized by meconium ileus, steatorrhea with absence of growth and weight increase, progressive bronchiectasis, and abnormal electrolyte concentrations in the perspiration. The concentration of sodium and chlorine in the perspiration is five times higher than normal, but there is hardly any change in the potassium concentration. It can always be shown that some blood relatives who show no clinical signs of the disease have the same changes in the perspiration. Klinke and co-workers (*Deutsche medizinische Wochenschrift*, 1958) made investigations that led them to conclude that the general disturbance consists in a change of the cell mechanism (probably of all cells) responsible for homeostasis. A chemical change in the secretion of the mucigenous glands causing increased viscosity of the mucus may also occur. It cannot be said whether this is a direct consequence of the disturbed osmotic cell mechanism or whether it is due to a secondary metabolic abnormality. Judged by clinical experience the latter could arise only on the basis of the general osmotic disorder.

Longevity of Erythrocytes.—If one applies only such methods for determining serum substances with auto-antibody action as the Coombs' test and cold agglutinin determination to detect hemolytically active factors in the serum of leukemic patients, these will only be found in rare cases. As all hemolytic syndromes are associated with a shortening of the life of the erythrocyte, which is proportional to the degree of development of the syndrome, the modern method of labeling the erythrocytes by means of Cr^{51} are, according to Bruschke and Hennemann (*Deutsches Arch. klin Med.* **205**:263-275, 1958), a safe diagnostic measure to determine the hemolytic factor of anemias in leukosis. The use of this method in six patients with myelosis, three with lymphadenosis, and one with paramyeloblastic leukemia showed that in nine of these patients the life of the red blood corpuscles was shortened. One patient with lymphadenosis and the patient with paramyeloblastic leukosis, who showed a hemolytic syndrome due to antibodies with positive results of Coombs' test, did not differ from the other eight patients as regards longevity of the erythrocytes. In these two patients the degree of the anemia did not seem to depend on the antibody findings. No interdependence between the shortened lifetime of the erythrocytes and the degree of the anemia or the size of the spleen could be found.

INDIA

Meprobamate in Psychiatry.—M. L. Joshi and coworkers (*Journal of the Association of Physicians of India*, vol. 6, Oct. 4, 1958) used meprobamate to treat 29 outpatients with various psychiatric disorders (11 with agitated depression, 7 who had somatic manifestations of anxiety, 5 who had excessive, organically based psychomotor activity, 4 with schizophrenia, one with a compulsive obsessive neurosis, and one with hypochondriasis). The period of study lasted three or four weeks so that there was little chance to establish rapport or to change environmental factors; 23 received meprobamate tablets alone and 6 were given meprobamate as well as placebo tablets containing 3 mg. of quinine each in order to imitate the bitter taste of meprobamate. The meprobamate was given in three equal doses of 1.2 to 1.4 Gm. a day. Complete relief was obtained in 6 patients, marked improvement in 3, moderate improvement in one, slight improvement in 9, and no improvement in 10. Of the 11 patients with agitated depression 4 obtained complete relief, 1 was moderately improved, 2 showed slight improvement, and 4 did not respond. Of the six who had anxiety with somatization one showed marked improvement, one moderate improvement, three slight improvement, and one was not benefited.

Of the two patients with excessive, organically based psychomotor activity, one improved markedly while the other showed no improvement. The response in the rest of the patients in the series was negligible. Of the six who received meprobamate and a placebo in alternate weeks, one showed marked improvement on meprobamate alone, but returned to the original state when the meprobamate was stopped and the placebo started. The favorable response returned when meprobamate therapy was resumed. In the other five the results were not so clear cut. Improvement occurred whenever either of the tablets was used but stopped as soon as the tablets were withdrawn. In patients with agitated depression, the improvement was characterized by lessened irritability, a general sense of well-being, and a decrease in morbid preoccupation with symptoms; there was a sense of relaxation with greater ability to concentrate and a return to more active social life. These changes were noticed within a few days of starting treatment. On the whole, patients with excessive psychomotor activity showed the greatest unfavorable response; eight, receiving 800 mg. of meprobamate three times a day, suffered from drowsiness, giddiness, weakness, and ataxia, but these symptoms

disappeared when the dosage was reduced. The results did not improve significantly when dosage was increased from 3 to 6 tablets a day.

Serum Electrolytes at Different Blood Pressure Levels.—Mathur and Wadhawan (*Journal of the Association of Physicians of India*, vol. 6, October, 1958) reported that although there is sufficient experimental evidence to indicate that the sodium chloride content of the intracellular tissue of hypertensive experimental animals is increased, and hypertension is thus generally believed to be associated with alteration of intracellular electrolytes, it is not known definitely whether these changes are associated with similar changes in extracellular fluids and plasma. The authors studied 50 normal subjects and 30 hypertensive patients with similar dietary habits belonging to the same socioeconomic group. Patients showing evidence of cardiac decompensation or any other disease were excluded from the study. The serum sodium level was found to be higher in patients with hypertension than in normal subjects, and showed a tendency, neither constant nor significant, to rise with increase in the systolic blood pressure. A more definite increase in the serum sodium level was seen with a rise in the diastolic blood pressure, the former varying directly with the latter. The serum potassium levels were slightly lower in the hypertensive patients as compared to the controls, but there was no definite relationship between systolic and diastolic readings and the level of serum potassium.

Intrapleural Pressure in Ascites.—P. N. Laha (*Journal of the Indian Medical Association* vol. 31, Nov. 1, 1958) studied the changes in intrapleural pressure in 20 patients with ascites caused by portal cirrhosis. The modified Lillington and Pearson pneumothorax apparatus was used to measure the intrapleural pressure, and the site of the readings varied from the second to the fifth right intercostal space depending on the level of the diaphragm. In the first 10 patients the intrapleural pressure was measured before and soon after paracentesis abdominis and in the other 10 before and 24 hours after drainage of the ascitic fluid. The intrapleural pressure was found to be within normal range during both inspiration and expiration in 10 patients. In 16, including the first 10, it was normal during inspiration; and in 11, also including the first 10, it was normal during expiration. In six the intrapleural pressure was normal during inspiration but positive during expiration; less than normal during inspiration with normal pressure during expiration in one, and less than normal during inspiration and positive during expiration in three. This modification in one phase of respiration was due to a compensatory emphysema in those patients in whom ascites produced mechanical obstruction to respiration.

The degree of modification in the intrapleural pressure varied with the degree of emphysema, the modification being slight and only on expiration when the emphysematous changes were slight, except in one patient in whom the only modification was a diminution in intrapleural pressure below the normal minimum on inspiration with normal pressure on expiration. The changes in intrapleural pressure in emphysema were due to alteration in lung elasticity produced by this condition. The readings taken soon after draining of the ascitic fluid did not show any significant alteration in the intrapleural pressure from the preparacentesis level. The changes in intrapleural pressure in five patients due to compensatory emphysema also remained about the same after drainage of the ascitic fluid. Thus the compensatory emphysema with its resultant alteration in pulmonary function, reflected in the intrapleural pressure, did not revert back to normal soon after relieving the mechanical obstruction to respiration caused by the ascitic fluid. The readings for intrapleural pressure taken 24 hours after paracentesis showed that there was no significant change, while the modification of intrapleural pressure in one or both phases of respiration, due to compensatory emphysema of the lungs, remained practically unchanged in three patients but showed significant variation in two from the positive pressure during expiration to normal figures after draining of the fluid. Thus the compensatory emphysema reverted back to normal in two patients 24 hours after relief of ascites, although clinical signs of emphysema persisted. The duration or amount of ascites had no significant correlation with the modifications of intrapleural pressure.

Nicotinic Acid in Optic Atrophy.—Mathur and Gupta (*Journal of the Indian Medical Association*, vol. 31, Nov. 1, 1958) used nicotinic acid to treat four patients with optic atrophy resulting from tuberculous meningitis. Three were under 5 and one was 24 years of age. The children were given nicotinic acid orally in daily doses of 100 mg. and the adult was given 300 mg. daily. The treatment was continued for six months in one and four months in the other three. Two of the patients showed definite improvement during the course of treatment. They were followed up for three months and were declared cured. The other two did not improve during the course of treatment; probably irreversible changes consequent on the longer duration of the optic atrophy before treatment was started or some other unknown factor was responsible for the failure of their treatment. K. J. Vyas gave eight patients, all children between 2 and 8 years of age whose blindness was due to tuberculous meningitis, nicotinic acid by mouth. They were given an initial dose of 100 to 150 mg. daily followed by 50 mg. daily. Five had normal vision at the

end of treatment. In one case the drug was given for only 12 days and the absence of response was due to the short duration of therapy. In another case the failure may have been due to irreversible damage to the optic nerve or the occipital lobe, as the child was unconscious for three months and had severe neurological damage at the time of admission. In the third case failure of response may also have been due to severe neurological damage. Improvement in those who recovered their vision started within 17 days of treatment except in one patient who could see close objects only after 47 days of treatment. Temporary side-effects were seen in only one patient, a child who developed a flush all over the body lasting for over an hour after the administration of nicotinic acid.

Tuberculosis in Contacts.—Warawdekar and Shah (*Indian Journal of Medical Sciences*, vol. 12, October, 1958) made a mass miniature roentgenographic study to determine the incidence and morbidity of pulmonary tuberculosis in home contacts of patients suffering from active pulmonary tuberculosis; 1,605 unselected patients suffering from active pulmonary tuberculosis were included in the study. All the members in the families of these patients (7,305) were investigated with mass miniature roentgenography. The positive findings were grouped into the following categories: primary complex; progressive primary complex; pleural effusion; active pulmonary lesions such as bronchopneumonic, pneumonic, cavitating, and fibrotic; quiescent pulmonary lesions; endobronchial tuberculous lesions; calcified lesions; and enlarged tuberculous lymph nodes. Of the 7,305 contacts 514 (7%) were found to be positive for tuberculosis; 44% of these were men, 28% were women, and 28% were children. Of the positive contacts 409 had active pulmonary tuberculosis and in 105 the disease was either healed or arrested. A high incidence of progression of the primary lesion was seen in the age groups under 4 and between 5 and 7 years of age. Active pneumonic and cavitating lesions were most common in adults but most had mild lesions. The study revealed a high incidence of tuberculosis requiring active treatment among contacts.

Antihypertensive Therapy.—H. N. Singh (*The Indian Practitioner* vol. 11, October, 1958) treated 50 patients who had hypertension with tablets containing 0.1 mg. of reserpine and 10 mg. of dihydrazinophthalazine. Patients with a systolic pressure above 150 mm. Hg and diastolic pressure above 100 mm. Hg were selected for trial. Blood pressure readings were repeated on the seventh day of treatment, in the third week, and at the end of treatment. The dose given to most patients was one tablet three times a day but larger doses were given when the initial pressure was high or the patient did not respond to this dose. The minimum number of tablets used daily was 3 and the maximum 12. The minimum period of treatment was 4 and the maximum 97 days. The series included 10 patients with no cardiac enlargement, 4 with an enlarged heart, 14 with congestive cardiac failure, 3 with renal failure, 11 with cerebral thrombosis, and 8 with other concomitant diseases.

The results on the whole were satisfactory; 56% showed good results with a fall of 20 mm. Hg (systolic or diastolic), 16% gave a fair response, and 28% had a poor result. A gradual fall in systolic and diastolic levels was noticed in the course of treatment. The average time taken to reduce the diastolic pressure by 20 mm. Hg was six days and the average number of tablets required to bring this about was 30.4. The side-effects of reserpine were minimal even with large doses and consisted of mild drowsiness and occasional nasal congestion. Only a few patients complained of infrequent headaches due to the dihydrazinophthalazine. Subjective and objective symptomatic improvement was noticed in all those showing appreciable reduction in their blood pressure.

Tropical Eosinophilia.—M. Viswanathan (*Journal of the Association of Physicians of India* vol. 6, October, 1958) treated 20 patients who had tropical eosinophilia with 750 mg. of diethyl carbamazine in a single intramuscular injection. The youngest patient was 18 and the oldest 45 years of age. All had pulmonary signs and an absolute eosinophil count of over 2,000 per cubic millimeter. The duration of symptoms varied from 4 to 26 weeks. In 16 patients the presenting symptom was cough and the other 4 complained of wheezing and breathlessness resembling bronchial asthma. Hemoptysis was noted in two, a sense of constriction in the chest in eight, and a low-grade fever in two. Scattered crepitations and occasional rhonchi were the commonest findings. The liver was enlarged and tender in one. The leukocyte count ranged between 10,000 and 52,000 per cubic millimeter. Eosinophils formed 25 to 91% of the total leukocyte count and the maximum absolute eosinophil count was 47,000 per cubic millimeter. All patients showed increased lung markings on radiologic examination and the typical mottling was seen in seven. There was no correlation between the esosinophil count and the roentgenologic findings. The total and differential white blood cell counts were repeated on alternate days after the single injection till normal values were obtained. The cough and wheezing showed signs of abatement within 48 to 96 hours of injection. Four had an aggravation of symptoms in the first 24 hours but definite signs of improvement appeared within 72 hours. Symptomatic relief was complete within a week in all but one.

A rapid fall in the total leukocyte count corresponding to the fall in eosinophil concentration was noticed within 4 to 6 days in 18 patients, and all of these had normal blood cell counts at the end of 10 to 12 days. In one the blood cell count took three weeks to return to normal although symptomatic relief was evident within one week. The patient with an absolute eosinophil count of 47,000 per cubic millimeter had 18,000 eosinophils at the end of 10 days and was given a second injection of 500 mg. His eosinophil count returned to normal in two more weeks. No toxic symptoms were noted in any of the patients.

Clinical Trial with Acetazolamide.—Bhattacharya and Bhuyan (*Journal of the Association of Physicians of India* vol. 6, October, 1958) treated a series of 15 patients (6 with cirrhosis of liver, 6 with nutritional edema, and 3 with hypertensive disease and congestive cardiac failure) with acetazolamide. Their ages ranged from 15 to 70 years. The patients were given a salt-free diet but fluid was not restricted. Those with nutritional edema were given an extra egg and a pint of milk. The protein intake of cirrhotic patients was restricted while the drug was being given and they were encouraged to drink glucose water. No digitalis was given to cardiac patients, and mercurial diuretics were not used during the period of trial. This regimen was observed for three days and the fluid intake and urinary output measured on the third day and taken as a base. Acetazolamide was then started in a dosage of 250 mg. daily by mouth or intravenously in a 25% glucose solution in the morning for three consecutive days. If additional treatment was required, due to the edema, the drug was given for another three days after an interval of three days. The fluid intake and urinary output were measured during the treatment and on the day immediately after its completion.

The average daily diuretic response showed an increase of 52.6, 49.0, and 50.7% over the base output on the three consecutive days of the trial. The net water loss due to acetazolamide averaged 62.9, 65.4, and 58.3% of the fluid intake on each day of the trial. Thus a good diuretic response was obtained with this drug. The effectiveness of a single daily dose was about the same for the three days, but the individual responses showed some variation; 10 patients had more than a 25% increase in output; 2 had the same; and 3 a decreased output. The final result, taking into consideration the response on the fourth day, was excellent in six, good in two, fair in three, and poor in four. The only side-effects noticed were a burning sensation in the abdomen and abdominal pain in the patients with nutritional edema, and these were mild and transitory. None of the patients with cirrhosis or nutritional edema showed signs of impending hepatic coma, although one cirrhotic patient was given two courses of treatment. Some of those with cirrhosis complained of nausea, anorexia, and abdominal pain. No harmful effects were seen in the peripheral blood. The blood urea level did not rise after completion of treatment, urinalysis showed no changes, and no skin reaction occurred. The diuresis persisted on the fourth day even when no drug was given.

Entamide for Amebiasis.—Sanjivi and Thiruvengadam (*Journal of the Association of Physicians of India* vol. 6, October, 1958) gave Entamide (dichloracet-4 hydroxy N methyl anilide) by mouth for 10 days to 30 patients who were passing cysts of Entamoeba histolytica in their stools. Three dosage schedules were used; 15 mg. per kilogram of body weight was given to 13 patients (group 1); 25 mg. per kilogram to 6 (group 2); and 40 mg. per kilogram (group 3). In two the finding of amebic cysts in the stools was accidental, one being treated for bronchiectasis and the other for vitiligo. Associated ankylostomiasis was present in one and ascariasis in another. The drug was given in three equal doses. Disappearance of cysts from stools occurred by the fifth day of treatment in all patients. The period required for eradication of cysts from stools averaged four days in group 3, four and six-tenths days in group 1, and six and eight-tenths days in group 2. The abdominal pain present in 24 was relieved in all but 5 and 6 of the 8 who had loose stools were relieved of this symptom. The amebic hepatitis present in two was unaffected by this drug, although the cysts disappeared from stools as in all other patients.

One of the patients in group 1 had a recurrence of abdominal pain and reappearance of cysts in his stools six months after the first course. He was then given the 40 mg. per kilogram dosage schedule, which gave complete relief, and nine months later there had been no recurrence. One of the patients in group 2 had a recurrence one month after the first course. He did not respond to another course with the larger dosage and was later given a different amebicide. He had developed hepatitis between the two courses of Entamide. All the rest of the patients in the series have been free of symptoms. The relapse rate for the series was 11.3%.

Another series of 26 patients suffering from acute amebic dysentery and passing vegetative forms of E. histolytica in their stools was also given the drug to compare its effect on the two phases of the parasitic infestation. Of these 12 had a previous history of amebic dysentery. The duration of the dysentery varied from two days to 18 months. Nine had concomitant amebic hepatitis, three also had ascariasis, one had strongyloidiasis and filariasis with chyluria, and another had chronic malaria. Sixteen patients (group 4) were

given 15 mg. of the drug per kilogram of body weight. The dose was later raised to 25 mg. per kilogram in 7 of these; 10 (group 5) were given 40 mg. per kilogram in three divided doses. The usual period of therapy was 10 days but the drug was discontinued earlier if the dysentery increased in severity or the general condition became worse.

In 12 patients in group 4 blood and mucus disappeared from stools in four days and in 10 the stools became formed on the seventh day. The disappearance of the trophozoites from the stools occurred, on an average, on the third day in 12 patients. In four the drug had to be discontinued and emetine given because of the severity of the dysentery. In two of the patients in group 5 the drug was discontinued after a week and emetine started; in the other 5 the trophozoites disappeared on about the third day and the blood and mucus on the fifth day. In 3 patients in group 5 emetine had to be substituted for the Entamide and in the rest trophozoites disappeared from stools on the fourth day and blood and mucus on the fifth day. The amebic hepatitis and other incidental infections were not affected. The rate of relapse was 48.5%. No side-effects attributable to the drug were noted.

Effects of Sodium on Normotensive and Hypertensive Subjects.—Mathur and Wadhwan (*Journal of the Association of Physicians of India* vol. 6, October, 1958) observed the levels of serum sodium and potassium and the renal excretion of sodium on sodium restriction and sodium load in the diet of 10 hypertensive and 10 normotensive subjects. The hypertensive subjects suffered from essential hypertension, benign or malignant, patients with hypertension associated with kidney disease or cardiac decompensation being excluded from the study. All were given throughout the period of investigation a constant diet consisting of 7 oz. of rice and 4 oz. of curd morning and evening. The low sodium content of rice was an advantage, while the diet was simple and easily available and yielded 30 Gm. of protein, 312.2 Gm. of carbohydrate, 7.2 Gm. of fat, 130 mg. of sodium, and 1,498 calories.

While making observations after loading with sodium, the diet was supplemented with 5 Gm. of sodium chloride given in capsules. Twenty-four-hour urine samples were collected on the first day to determine the sodium content. The rice and curd diet was then started and given for three days during which the urine was collected daily for sodium estimation. The diet was then loaded with sodium chloride by giving the capsules with the basic diet for three days during which the urine was again collected daily for sodium estimation. Samples of blood were also taken initially and on sodium withdrawal and loading to determine the serum sodium and potassium levels. The mean urinary excretion of sodium prior to salt restriction was comparable in the two groups, although marked individual variations were seen. After withdrawal of sodium the amount of sodium excreted in the urine showed a rapid fall in both groups and there was no appreciable difference between them. On loading with sodium, however, the hypertensive patients showed a tendency to reject more sodium and water than did the normotensive subjects. The levels of electrolytes in the serum showed no appreciable change on withdrawal or loading.

SWEDEN

Knee-Joint Disarticulation.—On the basis of the results in 14 patients on whom disarticulation of the knee was performed, the following conclusions were drawn by Lars Unander-Scharin in *Nordisk medecin* (**60**:41, 1958). A large, horizontal weight-bearing surface for the prosthesis was obtained. The skin, soft tissues, and bone at the end of the stump adapted to weight-bearing earlier. The muscular control of the stump was better, since the attachments of the muscles remained intact. The leverage on the prosthesis was more effective, because the stump was longer and its end firm and unyielding. The prosthesis was attached to the club-shaped end of the stump by means of a lacer. Shoulder straps or belts were not needed. These devices were also unnecessary for limbs attached by means of suction sockets. Adequate circulation in the stump could be maintained, provided the popliteal artery was ligated below the branching off of the superior genicular arteries. In children growth of the lower part of the femur occurred in 70%, which meant that the length of the stump would remain unchanged in relation to the femur of the sound leg, and thus the problems connected with changes in the shape of the stump would not arise. The making of the prosthesis did not involve any great difficulty. In most cases the patient soon became accustomed to wearing an artificial leg and found it easy to resume his old activities.

Cow's Milk Formula for Infants.—Lars Söderhjelm in *Nordisk medecin* (**60**:42, 1958) proposed a formula for infants of which 50 to 67% was skimmed milk, about 4% was cane sugar, about 1% was oat or wheat flour, and 2 or 3% was a fat mixture with linoleic acid, which contained additional iron, and vitamins E, C, and B. If desired the mixture can be acidified with citric acid. This formula contains about 600 calories per liter. It is not "humanized" to any great degree and does not contain any bifid factors. The content of lactose is low and that of calcium high in comparison with breast milk, but experience at the pediatrics section of the Skellefteå hospital indicated that similar mixtures were well tolerated and, moreover, they are relatively cheap.

Sedimentation Rate During Pregnancy and Puerperium.—The sedimentation rate (Westergren) was measured in 1,082 healthy pregnant women and in 532 pregnant women with various disorders due to disease, and reported by Clarence Malmnas in *Opuscula medica* (3:9, 1958). The rate rose from a mean of 11 mm. in the 2nd month of pregnancy to 48 mm. in the 10th month. The mean sedimentation rate was highest in the first week of the puerperium (54 mm.) and then rapidly fell in the following weeks, but six weeks after normal parturition it was still somewhat higher than in nonpregnant controls (11 and 8 mm. respectively). The mean sedimentation rate in toxemia of pregnancy was significantly higher than in normal pregnancy and the higher rates in the toxemic group appeared before such other signs of toxemia as proteinuria, edema, and hypertension. In pregnant women with backache of obscure cause, in anemia of pregnancy, abortion, premature birth, and multiple pregnancy the mean sedimentation rate was significantly higher than in normal pregnancy at the same month.

Action of Nicotinic Acid.—The simultaneous equimolar increase in the serum iron and so-called indirect bilirubin after intravenous injection of nicotinic acid can be explained by indirect hemoglobin breakdown. The increase in serum iron and in serum bilirubin after the intravenous injection of 50 mg. of nicotinic acid was studied in 10 normal subjects, 23 patients with hypochromic anemia, 19 with anemia of hyperthyroidism, 23 with polycythemia, and 2 with acholuric jaundice by Karl Gydell (*Acta med. scandinav.* **162**:9, 1958). The increase in the two serum components within one hour of the injection was found to be abnormally small in the two groups with anemia and abnormally large in the patients with polycythemia. The increase in the serum bilirubin and serum iron in relation to the hemoglobin level was by far the greatest in the two patients with congenital hemolytic anemia. Exogenic iron and bilirubin loading (after intravenous injections) was compared with endogenic (nicotinic acid induced) loading. As calculated from the relative increases in serum bilirubin and serum iron during the first hour after the injection and by the size of the plasma volume, the amount of hemoglobin broken down was about 0.5 Gm. in normal subjects. In one patient with congenital hemolytic anemia the amount was as much as 3.8 Gm.

Nonuniformity of Pulmonary Ventilation.—Six patients with chronic obstructive pulmonary emphysema, uncomplicated by airway infections, bronchospasm, or right heart failure, were studied by Arend Bouhuys and co-workers (*Acta med. scandinav.* **162**:29, 1958) with an open-circuit nitrogen washout method to determine the extent of nonuniform ventilation and the general washout efficiency. The fall of the end-tidal nitrogen concentration and the amount of nitrogen washed out per breath were measured simultaneously. No consistent differences between the volume and percentage graphs were demonstrated, and for clinical purposes it seems to be sufficient to study only the fall of the end-tidal nitrogen concentration. Four of these six patients showed clearly pathological degrees of unequal ventilation and decreased washout efficiency. The other two had only slightly decreased general efficiency and borderline normal degrees of nonuniformity in spite of spirographic signs of emphysema. One older subject showed completely uniform ventilation in spite of some evidence of diminished ventilatory reserves. One patient had a normal degree of nonuniformity and normal washout efficiency after pneumonectomy.

TURKEY

Viral Exudative Pleuritis.—Dr. Sevki Sonsuz of Izmir (*Forum Medicum*, vol. 2, p. 303) in the internal medicine department of the Canakkale Military hospital within a period of about eight months treated 562 patients with viral exudative pleuritis. The disease began with prostration, chilly sensation, rhinitis, and bronchitis as in influenza. Occasionally high fevers (39 to 40 C [102 to 104 F]) were recorded but frequently moderate fevers were observed. The temperatures of some of these patients were normal. Most of them complained of pain in the side. Dulness to percussion over the lower parts of the lung was found in most of the patients. Pleural puncture revealed serofibrous fluid. All of the exudate withdrawn from these patients gave a positive Rivalta's reaction. At first tuberculosis was considered but since this disease does not occur in such epidemic proportions, another cause had to be sought. Furthermore, results of guinea pig inoculation tests were negative for tuberculosis.

In many of the patients roentgenograms showed no abnormal findings even though after x-ray examination 70 cc. or more of exudate could be removed from the pleural space. Probably in exudative viral pleurisy the reason for the transparency to the x-rays was the inadequacy of colloidal substances in the fluid to produce opacity. A pleurisy transparent to x-ray is not necessarily of viral origin. Sometimes it is impossible to identify a tuberculous pleurisy by roentgenography but in such patients the Rivalta's reaction is negative. When this reaction becomes positive the exudate is opaque. Fresh transudates are also not opaque to the x-ray. Viral exudative pleurisy may be either endemic or epidemic. It occurs especially during autumn and winter when viral infections are prevalent, and its course is usually benign. Explorative pleural punctures are more valuable than x-ray examinations in the diagnosis.

UNITED KINGDOM

Death Certification of Children.—A survey of the accuracy of causes of death given to the registrar at a children's hospital showed that almost half the certifications were not correct as judged by the final diagnosis. Emery and Irvine carried out 150 consecutive postmortem examinations on the bodies of children dying in a Sheffield teaching hospital (*Brit. M. J.* **2**:1510, 1958). The physician in charge had previously recorded his opinion of the cause of death based on the clinical findings. The ages of the children varied from a few hours to 12½ years of age. In 55% of cases the clinical findings agreed with those found at autopsy, or differed in only minor respects. In 40% the pathological examination necessitated a complete revision of the stated cause of death. In 5% the cause of death given by the physician was not substantiated at autopsy, nor was any adequate cause of death found on grounds of pathological study. As the deaths occurred in a teaching hospital, it was considered that certification was as accurate as it could be on the basis of purely clinical data.

Clinical Trials on Children.—A question about clinical trials on children was raised in the House of Commons recently. Mr. Swingler, a Labor member, asked the Minister of Health if he had considered the report of a clinical trial in which mentally defective children were used as controls. Had the consent of the parents been obtained, he asked, and what assurance was there that no harm would result to the children? The Minister replied that parental consent had not been obtained, although it should have been, but that the drug used in the trial had no harmful effects. Mr. Swingler said he raised the same question 15 years ago, when children were used in trials with penicillin without the consent of their parents. He considered that this was wrong and that the hospital authorities should be advised on the matter. The Minister replied that a memorandum on the subject had been sent to the Medical Research Council and that investigations of this kind involve medical and ethical problems not susceptible to control and regulations. Another member pointed out that a number of promising research projects involve free access to patients. The Minister concluded by saying that there should be the greatest possible freedom from detailed supervision in clinical research in hospitals.

Physical Activity and Coronary Disease.—In Britain, coronary thrombosis, angina, and arteriosclerotic myocardial degeneration are responsible for about 25% of all deaths in men over 40. Investigations into the causes of coronary heart disease have been directed mainly to an assessment of the significance of intravascular thrombosis, defects in blood coagulation, hormonal factors, and physical activity. On the basis of observations on deaths from ischemic heart disease in men in various occupations, Morris and co-workers advanced the view that those engaged in physically active work have a lower incidence of ischemic heart disease than those in sedentary occupations. With the cooperation of several pathologists Morris and Crawford have obtained further data in support of this view (*Brit. M. J.* **2**:1485, 1958). All departments of pathology in the hospitals of the National Health Service were invited to contribute data on the condition of the coronary arteries and myocardium in 5,000 men aged 45 to 70 coming to autopsy. There were 1,200 deaths from coronary heart disease, 1,000 from conditions with a high prevalence of coronary artery disease, and 2,800 from miscellaneous conditions having no particular association with coronary artery disease. In the 3,800 autopsies performed on men dying from some cause other than coronary disease twice as much ischemic myocardial fibrosis was found in men engaged in light work as in those doing heavy work. Large healed infarcts were three times commoner in light workers than in heavy workers, and four to five times commoner in men between the ages of 45 to 60 years, but only two to three times commoner between the ages of 60 and 70 years. Thus ischemic myocardial fibrosis was commoner in men in light occupations and appeared in them at an earlier age.

The prevalence of coronary atheroma in both groups was high, although not related to physical activity or occupation. Coronary narrowing was also common, irrespective of occupation, but occlusion of a main coronary artery, complete or nearly complete, was commoner in sedentary and light workers than in those engaged in active and heavy work. In the presence of coronary narrowing and occlusion those in light occupations showed more ischemic lesions of the myocardium than did active and heavy workers. The expected relation of ischemic myocardial fibrosis to social class was confirmed, the rate falling 13.3% in class 1 (professional and managerial workers) through 10.5% in class 3 to 7.8% in class 5 (unskilled workers). This trend disappeared, however, when the social classes were broken down into categories of physical activity. Morris and Crawford put forward the hypothesis that physical activity is a protection against coronary heart disease. Men in physically active occupations suffer from it less during middle age; when it does occur it is less severe; and they develop it later in life than men engaged in sedentary occupations. Habitual physical activity was a general factor of cardiovascular health in middle age, and coronary heart disease was in some respects a deprivation syndrome or deficiency disease. In the investigation, the hearts of sedentary and light workers showed lesions comparable to those in the hearts of heavy workers 10 to 15 years older.

Hula-Hoop Syndrome.—The widespread pastime of wriggling hula-hoops around the waist has given rise to what has been called the hula-hoop syndrome. A number of children and young adults have complained of pain at the side of the neck associated with a pain in the upper abdomen. Both are aggravated by movement and in a few the pain is sufficient to produce torticollis. There is a varying degree of reduced movement of the cervical spine, especially rotation, which is limited by pain, and there is spasm and tenderness in one or both of the sternocleidomastoid muscles, the cervical portion of the trapezius muscle, and the paravertebral muscles in the cervical region. There is also tenderness, on palpation of the epigastrium and below the costal margin, which is aggravated by leg raising. The syndrome has been confused with poliomyelitis and meningitis. An active child complained of pains all over and inability to walk. She had moderate neck rigidity, was unable to sit up unsupported, and her lower leg movements were slow and painful. The lower limb tendon reflexes were diminished and the back muscles were tender, especially in the midthoracic region. A provisional diagnosis of poliomyelitis was made, but changed to benign lymphocytic meningitis when the child was hospitalized. These diagnoses were proved incorrect by a normal spinal fluid and rapid recovery of the patient with rest. The symptoms were due to using a hula-hoop at waist and neck level.

Noise in Hospitals.—An inquiry was made into unnecessary noise in hospitals by the King Edward's Hospital Fund for London. A questionnaire was sent to more than 2,000 patients in 15 hospitals for their comments. Many hospitals in large cities are located in areas where the roar of traffic is continuous, but this does not seem to worry most patients, at any rate by day, although at night and in the early morning it may be disturbing. Most of the irritating noise occurs in or just outside the hospital ward and is due to noisy equipment or thoughtless staff. Occasionally patients stated that noisy milk crates and refuse collectors were disturbing, or that they could not sleep because of noisy passersby at night or because of a neighboring dance hall or club. On the other hand nearly half the patients questioned stated that they were not bothered by noise. This is surprising, as the sick and unoccupied patient would be expected to be more sensitive to external stimuli than the normal person, but some of the patients may have been unable to express their views. Telephones, elevators, and carts are a frequent source of noise in hospitals. Adjustments can be made to elevators and carts, but the only solution to the telephone nuisance is to change the call system. Clanging metal bowls can be replaced by plastic ones. Rubber-soled shoes can prevent the clatter of nurses' feet, particularly at night, and noisy manic patients can be moved to side wards, soundproofed if necessary. These are some of the methods suggested for reducing hospital noises.

Prednisolone for Asthma.—The results of a clinical trial with prednisolone in the treatment of a selected group of 90 chronic asthmatics were described by Brown (*Lancet* **2**:1245, 1958). Only asthmatics who had had chronic bronchospasm for at least a year and who had proved refractory to all other treatment for at least a month were included in the trial. Cases of severe bronchial infection and bronchospasm of cardiac origin were excluded. The dose given was 5 mg. three times a day for a week, followed by reassessment and adjustment of the dose, which was reduced to a level sufficient to keep the patient free from wheezing. Any acute spasm was treated by increasing the dose rapidly until it was controlled. It was not thought safe to introduce placebo tablets into the trial because of the well-known dangers of suddenly withdrawing steroids. There was a striking improvement in those patients with eosinophils in the sputum. In general, the greater the number of eosinophils, the more certain was the result; 63% of the patients with eosinophilic sputum showed complete remission under treatment with prednisolone and nearly 8% showed partial relief. Of those with few or no eosinophils 5% showed partial or complete relief. The results thus indicated that in the absence of an eosinophilic sputum a satisfactory response with prednisolone is unlikely. Although the steroid is effective in suitable cases, it never does more than suppress the asthmatic state. This therapy does not cause the disappearance of eosinophils from the sputum, but greatly reduces their concentration.

Unnecessary Use of Penicillin.—Anderson showed that the common practice of using penicillin after operations for septic lesions of the hand is unnecessary in most cases (*Brit. M. J.* **2**:1569, 1958). A series of 357 patients with septic hand lesions were given without bias one of three treatments: surgery alone, surgery combined with penicillin by mouth, and surgery with depot penicillin. The conditions dealt with were paronychia, onychia, pulp and other abscesses, septic blisters, and chronic infections that had lasted a month or more before coming under treatment. Attention was focused principally on the rate of healing after the evacuation of pent-up pus. The criteria accepted for healing were a completely dry epithelized wound, full function of the affected part, and no need for further dressings or treatment. The oral dose of penicillin was 1,200,000 units daily in divided doses. Depot penicillin was given intramuscularly morning and evening until the wound had almost healed as a preparation containing 300,000 units of procaine benzylpenicillin and 100,000 units of sodium benzylpenicillin. The average healing times in the three groups were 9.4, 9.5, and

9.2 days respectively. Anderson concluded that careful clinical examination, accurate diagnosis, and careful repair are of greater importance than routine preoperative chemotherapy. Antibiotics do not hasten healing in septic lesions of the hand which require surgical treatment, provided that a careful surgical technique is based on an anatomically accurate diagnosis. Penicillin may be useful in selected cases, however, particularly in web abscesses. The judicious use of penicillin is a more effective counter to the emergence of resistant organisms than is recourse to other antibiotics.

New Anthelmintic.—Goodwin and co-workers (*Brit. M. J.* **2**:1572, 1958) compared a new anthelmintic, bephenium hydroxynaphthoate, with tetrachloroethylene in the treatment of 284 patients with hookworm infection in Ceylon. The effectiveness of treatment was judged from the number of hookworm eggs present in 1 ml. of feces before and four days after treatment. The drug was given early in the morning and no food was allowed before or until at least two hours after administration. No purge was given. A single dose of 2 or 3 Gm., or multiple doses given on successive days or three times on the same day, cleared the hookworms and ova as effectively as tetrachloroethylene without producing the toxic side-effects of the latter. Bephenium hydroxynaphthoate was particularly suitable for the treatment of patients with advanced anemia, diarrhea, and heavy helminthic infection because of its low toxicity and because no purge was necessary. It could be given to patients in poor physical condition whereas tetrachloroethylene could not because the latter is unpleasant to take and produces dizziness and nausea. Bephenium hydroxynaphthoate was also found to be effective against roundworm infection, which was present concurrently in many of the patients. Roundworms are resistant to tetrachloroethylene.

Legal Actions in the Health Service.—In reply to a question in Parliament on the cost of legal actions taken by patients against physicians and nurses in the National Health Service, the Minister of Health said that since 1948, when the service started, up to March, 1958, the total amount paid in compensation was just over $2,500,000. In the first year of the service it was only $21,170; in the last year it was $325,170.

Punch Biopsy of Parietal Pleura.—Blind punch biopsy of the parietal pleura was used by Mestitz and co-workers for determining the nature of a pleural effusion or pleural shadowing of unknown cause (*Lancet* **2**:1349, 1958). They described the results of 228 pleural biopsies made on 200 patients, most of whom had an effusion at the time of investigation, which was done whenever possible before treatment was given. Aspiration and punch biopsy were performed in one operation. The complications encountered in the 200 patients were subcutaneous hematoma, pneumothorax, and secondary deposits along the needle track from a neoplasm. In addition to a full clinical examination including chest roentgenogram, the sedimentation rate, leukocyte count, and tuberculin reaction were determined; the sputum was examined for tubercle bacilli and malignant cells; and a differential leukocyte count, 48-hour culture, and culture or guinea-pig inoculation for tubercle bacilli in the pleural fluid were made. Histological examination of the biopsy material enabled the diagnosis of tuberculous pleurisy and malignant infiltration to be made. The method is simple and safe. Since it can establish the diagnosis in about 80% of tuberculous and 60% of malignant effusions, it is the most reliable diagnostic technique when tuberculosis is suspected. In the 228 biopsies there was only one false-positive diagnosis. Because this procedure may be the only way of making a definite diagnosis during life, it should be part of the initial investigation of every patient with a pleural effusion of uncertain cause.

Urge Medical Cards for All.—The British Medical Association is considering the desirability of all persons carrying a personal medical card which would give their blood group, immunizations they had received, whether they were allergic to penicillin or other drugs, and whether they were diabetics, needing insulin injections. The Central Consultants' and Specialists' Committee believes that such a card should be devised. It would be of particular value in those instances when a physician had to treat a patient who was unconscious and unknown to him. The 97% of the population registered with family doctors under the National Health Service (NHS) already has medical cards, but these do not include personal medical details. Even if such details were added, the few people who remain outside the NHS would still need such cards. Some patients, hemophiliacs, for example, already carry cards giving information about their condition. This is of great value when an emergency arises. "If the introduction of a personal medical card saved the lives of half a dozen people," said one doctor, "it would be well worth while."

Some physicians doubt whether each member of the public could be persuaded to carry such a card. They are opposed to any coercion of the public. A medical record such as that used in the Army, they say, would be too bulky. Advocates of the personal medical card agree that the public could not be compelled to carry it. It would be for each person to decide, but if he agreed, his family doctor could readily supply those facts which might prove lifesaving in an emergency. The advantages and difficulties of such a scheme are being examined by the Association's science committee. Issue of a personal medical card would require the approval of the Ministry of Health, which would be guided by its professional advisers.

New Secretary for the British Medical Association.—Dr. Angus Macrae has retired as secretary of the British Medical Association and has been succeeded by Dr. Derek Stevenson, who has issued a pamphlet entitled "Lines of Communication" which he hopes will be a regular feature, and with which he hopes to keep in closer touch with members on the periphery of the Association. In the first number he discussed the present stages of the profession's negotiations with the government for increased rates of pay.

Drug Bill Up Despite Levy.—When the government increased the National Health Service medicine charge from 14 cents a prescription to 14 cents an item in 1956 as an economy measure, it anticipated a decrease of $12,500,000 a year in its drug bill, but the bill has increased by more than $4,000,000 a year. This was reported by Dr. J. P. Martin of the London School of Economics and Mrs. Sheila Williams in the *Lancet* of Jan. 3. With the new charge of 14 cents an item the number of prescriptions dropped from 5.51 per patient in 1956 to 4.93 in 1957, the lowest figure since the start of the NHS. The number of prescriptions per form also dropped, but the average cost of each prescription rose sharply from 66.5 to 81.5 cents. Nearly half this increase was due to doctors prescribing larger quantities of drugs. For chronic patients such as diabetics, at least, this practice had the support of the Minister of Health. The cost of charges to patients rose from an average of 46.5 cents in 1956 to 69 cents in 1957, and the proportion of the drug bill borne by patients rose from 12.26 to 17.07%. Though the number of prescriptions fell by nearly 20 million, the total drug bill rose by nearly 17 million dollars. The new charge brought in $7,700,000 in revenue.

New Coagulant.—A new coagulant for treating hemophilia, antihemophilic globulin, consists of a white powder obtained from the blood of pigs and is nearly 20 times as potent in its antihemophilic properties as are human blood transfusions. So far the treatment can be used only once to save a patient's life, but there are hopes that soon a purified preparation will be available which can be used whenever it is needed.

Medical Ancillary Professions.—Last-minute opposition by physicians is likely to delay the achievement of state registration by physiotherapists, radiographers, chiropodists, and five other medical ancillary professions. The physicians claim that they have insufficient voice in the proposed scheme produced by the Ministry of Health. This scheme is the result of 10 years of investigation and negotiation. Leading the opposition to it is the British Medical Association, which says that no scheme would be acceptable which did not give the medical profession a greater influence in the training and ethical standards of the ancillary professions. The proposed scheme provides for a registration board for each profession, with a coordinating council governing them all. The B. M. A. and committees representing hospital consultants say that there should be more physicians on both the boards and the council. State registration would benefit both the professions concerned and the public. Only state-registered medical auxiliaries would be employed in the National Health Service.

Electrolyte Losses due to Purgation.—Coghill and co-workers (*British Medical Journal*, Jan. 3, 1959), starting with the axiom that diarrhea may result in excessive loss of serum sodium and potassium if the intake of these factors does not restore the deficiency, studied patients who had made a practice of taking purgatives regularly, resulting in persistent diarrhea, the drugs being those which act as irritants on both small and large intestines. The habit of taking cathartics is so widespread that it is remarkable that so few patients appear to suffer serious metabolic effects. Some persons developed chronic colitis, but others remained free of it even after 40 years of purgation, though chemical and radioisotope tests demonstrated electrolyte depletion in patients with symptoms such as profound muscular weakness, intestinal hypotonus bordering on paralytic ileus, and alkalosis associated with renal failure. Some who had developed ulcerative colitis did not regain good health until a section of the diseased colon had been removed, but those without a permanently inflamed intestine were much improved when the electrolyte loss was controlled.

Decoration of Anesthesia Room.—Dr. G. C. Steel, anesthetist to the Royal Free Hospital and other London hospitals for women, studied patients' reactions before being anesthetized (*British Medical Journal*, Jan. 3, 1959). He complains that the anesthesia room has tended to acquire the coldly utilitarian lines of the operating room and is frequently too small. A picture painted on the ceiling of the new anesthesia room at Chelsea Hospital for Women achieved its purpose of distracting apprehensive patients. It is a cheerful composite pastoral scene. Patients spread the news about the picture. One woman objected strongly to receiving her anesthetic in the corridor on the ground that she did not want to be done out of seeing the picture she had heard so much about. Only 10 of 100 patients did not notice the picture. Remarks on it were favorable (73), unfavorable (4), and noncommittal (23). The lighting is indirect, and thrown onto the ceiling. If premedication has been heavy, the effect of the mental diversion aroused by the picture is reduced.

CORRESPONDENCE

SEROLOGIC TESTS FOR SYPHILIS

To the Editor:—The persistence of syphilis as a major medical problem has stimulated continued serious study of all aspects of this problem. The article by Waring and associates, in THE JOURNAL, Dec. 13, 1958, page 2004, entitled "Biological False-Positive Results in Serologic Tests for Syphilis" does not, I feel, make a contribution to this problem because of serious defects in its planning and interpretation. The study reports that negative Treponema pallidum immobilization (TPI) test reactions were found in about 40% of 23 seroreactions referred for "diagnostic verification" on white patients. In 52 unselected Negro patients, no negative TPI reaction were found. One conclusion was that "the false-positive phenomenon is quite rare in the Negro race." No information is given in the article on the socioeconomic backgrounds of the two groups, though the boxed summary preceding the article states that the Caucasian patients "varied widely in socioeconomic background" and that the Negro patients were "thought to be a relatively homogeneous social and economic group."

If this bias in the selection of the two study groups was actually present, the difference in negative TPI rates could not be ascribed to racial factors. Another example of poor epidemiologic methods is the identification of these findings in 52 Negro patients with "the epidemiology of syphilis." Not only the small number of patients but their unrepresentative character for the general population exposed to syphilitic infection makes any statements concerning them valid only for them. It is hoped that better planned and controlled studies of all types will be forthcoming so that this important public health problem may soon be brought under complete control.

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To the Editor:—The small size of our study, commented on by Dr. Hyman, was acknowledged in the text; but we are prepared to retreat only in the face of larger numbers. The original study of the incidence of the false-positive reaction was the work of Moore (our reference 4), who deliberately chose white, upper income, private patients with positive reagin tests as his subjects. These persons were drawn from an area where syphilis is relatively less common than in other localities which might have been selected. False-positive reactions would therefore be expected more frequently than in samples of other social composition. It is eminently sensible to probe for a new phenomenon in a place in which it is likely to be found. We believe that the false-positive problem has been over-emphasized, and our study was planned (i. e., biased) to provide a look at the other side of the picture. We believe that the habits of our Negro patients involved a higher than average frequency of exposure to infectious syphilis.

We do not believe, nor did we state, that our Negro patients (or, incidentally, Moore's white patients) represented the "general population exposed to syphilis" referred to by Dr. Gold. We join Dr. Gold in rejecting the view that "racial factors" are involved—at least as the physical anthropologist understands the term "racial." Finally, objections are raised to the observation that the biological false-positive is "quite rare in the Negro race" and the validity of our epidemiologic notions in general. So far as our small study goes, *res ipsae loquntur.*

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THE PRACTICE OF MEDICINE IN CHINA

To the Editor:—It would be worthwhile for all members of the medical profession to read the article in the *Chinese Medical Journal* (77:413-426 [Nov.] 1958) concerning the management of burned patients from a Shanghai steel mill; it is entitled "The Fight to Save Steel Worker Ch'iu Ts'ai-K'ang's Life: A Summing-up Report by the Shanghai Second Medical College Committee of the Chinese Communist Party." This is the first time I have seen a medical journal devote a section to communist propaganda. The following excerpts from the article are self-explanatory.

> The outcome of this struggle has proved, once again, that a proletarian party, and only such a party, is capable of leading every kind of work, including the extremely exacting science of medicine. . . . The Party committee of the Shanghai Second Medical College analyzed the ideologic state of the doctors, and correctly pointed out that what could not be done in capitalist countries we could do, and what the capitalist literature did not record we would record. This is possible because our social system and theirs differ. The people burnt there are the exploited workers. The capitalist whose only concern is for profits and more profits will most certainly not expend money and energy to save a worker. No more would the intelligentsia who serve the capitalists. . . . During the two months fight to save comrade Ch'iu Ts'ai-K'ang the leading role played by the party convinced the senior doctors and they acknowledged with all their heart that: "It's true that diseases can be treated by Marxism-Leninism," and that "without the Party intellectuals like us could not possibly have broken out from the established rules of bourgeois experts. . . ."
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> It was truly said that in this fight to save Ch'iu Ts'ai-K'ang, on the one hand the doctors cured Ch'iu of his burns, but on the other hand, through this curing the doctors them-

selves were cured: cured of their blind reverence for foreign authorities, their blind faith in textbooks, their doubts in the Party and in the masses, their unrealistic approach to problems. . . . Recently our college established departments to study hypertension, schistomiasis and measles vaccination. In each of these departments there is a concurrent political head. Also communists and members of the Communist Youth League are in charge of the different research projects so as to expedite the intellectuals and their own proletarian remoulding and the advancement of their technology."

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CARDIAC EMERGENCY

To the Editor:—Dr. Carmichael's sketch with brief text in the Correspondence section of THE JOURNAL (**169**:176 [Jan. 10] 1959) has come to my attention. Since most cardiac standstills occur from myocardial failure due to rapidly progressive anoxia—stagnant, anemic, or histotoxic anoxia or an unfortunate combination of these—it might be well to dwell briefly on the vital issue of respiratory support. While Dr. Carmichael admits the proper sequence of events, he unhappily reverses this sequence at the bottom of his line cut, by placing "knife" over "airway." The need for respiratory support apparently is to be covered by providing a plastic airway, tacitly by-passing the issue altogether. What surgeon would think of opening the chest without the protection of an endotracheal tube, providing direct insufflation of the lungs with oxygen or air? Yet the patient about to die from hypoxia is expected to get along without this support. To maintain that an anesthetist is essential for the intubation of a flaccid patient is an attitude fatal to the success of cardiac massage. What, it may be asked, is the use of massaging a heart whose blood is bereft of oxygen? Having assisted in the training of more than 1,000 physicians, in the simple procedure of the direct intubation of the flaccid patient, I am satisfied that this preliminary to successful cardiac massage, with or without defibrillation, can be performed without difficulty.

In a technical procedure involving life and death, most of us hate to face the need to learn all about it at the time of our first exposure, and, yet, how many have seen the relaxed glottis, passed a tube into it, blown into this tube, and seen the lungs expand? How many have felt the relaxed heart in the hand, massaged it, and seen the blood pressure sustained and the rhythm restored by defibrillation? Such instruction, in an intensive form, with live clinical material is available and can be secured with but slight delay. Once the physician is experienced, this instruction provides a psychological and a medicolegal sense of security.

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LAW DEPARTMENT

MEDICOLEGAL ABSTRACTS

Governmental Hospitals: Examination to be Given Emergency Patient.—This was an action for damages against the administrator of a county hospital for alleged negligent conduct in the hospital's emergency room. From a judgment in favor of the defendant, the plaintiff appealed to the Supreme Court of Florida.

The deceased, clad only in trunks, was found about 1:30 a. m. stretched out on the lawn of the Dean Hotel in Miami. He was described by the police officer who found him as "unconscious." The police officer also stated that he detected a "slight odor" of alcohol, although the ambulance driver said he noticed none at all. The intern in the hospital's emergency room testified that the man's chest sounds and pulse were normal and that although not unconscious he was incoherent and his breath literally reeked with alcohol. He stated that someone told him that the man had been "found on the street," but he did not undertake to obtain any history of the situation and no roentgenograms were taken. After what appears to have been a relatively superficial clinical examination the intern released the man to the care of a nurse who returned him to the hospital police room for delivery to the police as a drunk. About 3 a. m. the police carried the man to a patrol car and conveyed him to the municipal jail.

The police officer testified that the man slumped over on the seat of the automobile as if his "back were broken." When placed on the elevator to carry him up to the jail, the man couldn't stand up but slumped down on the floor. He was put into a cell on a metal cot and left to himself. About 7 a. m. that morning he was found dead, death having been caused by air and hemorrhaging in the thoracic cavity resulting from the piercing of the cavity by about nine broken ribs.

The plaintiff, administrator of the deceased's estate, contended that the death of the deceased was the result of the defendant's failure to use reasonable care and skill in the hospital emergency room; but the trial court felt that the relationship between the death and such alleged negligence was too remote and speculative.

The Supreme Court admitted that the science of medicine is not an exact one and that physicians are not to be held liable for honest errors of judgment. To hold a physician liable it must be shown that the course which he pursued was clearly against the course recognized as correct by the profession. The responsibility and degree of care imposed upon the defendant hospital, said the court, is to be measured by the responsibility and degree of care imposed upon its employees, the intern and nurses in

the emergency ward. Instead of discharging the deceased as drunk after 15 or 20 minutes, should the intern have pursued a more thorough course of inquiry and examination under the circumstances?

No history of the man's condition and no facts leading up to his delivery to the hospital were obtained at any time. No roentgenograms were taken. The hospital director testified that if a patient was unconscious and unable to give his name and state how he was injured when delivered to the hospital, then releasing him in the same condition would in his judgment fall below the standard of care required under the circumstances. The physician supervisor of the emergency room testified that if a patient in the condition of deceased were admitted and could not give a history of his condition, and one could not be obtained, then he would certainly taken roentgenograms in an effort to form a diagnosis. He also testified that the fact that the deceased had a normal pulse rate was inconsistent with a state of intoxication. The pathologist who performed the autopsy said he could not conclusively state whether the broken ribs and their puncturing of the chest cavity were the result of a suspected fall from the second story of the Dean Hotel or from the failure to hospitalize the deceased and from permitting him to be moved about after examination in the emergency room. He did testify, however, that permitting a man with nine broken ribs to be moved and shunted about certainly would aggravate his condition and expedite his death.

On the basis of all this testimony, the Supreme Court was of the opinion that there was adequate evidence of negligence in the treatment, examination, and ultimate diagnosis of the deceased's condition to justify submission of the case to the jury. The judgment in favor of the defendant hospital was therefore reversed and the cause remanded for a new trial. *Bourgeois v. Dade County*, 99 So(2) 575 (Fla., 1957).

Expert Witnesses: Criteria of Competence.—This was an action for damages resulting from the alleged negligence of the defendant physician in removing or in recommending the removal of a small piece of metal from the plaintiff's body. The trial court, at the close of the plaintiff's evidence, directed a verdict in favor of the defendant so the plaintiff appealed to the United States court of appeals, fourth circuit.

The plaintiff operated a garage. While he was holding a steel automobile axle as it was being struck with a sledge hammer by his helper a small sliver of steel flew off and penetrated the base of the plaintiff's neck on the left side, near the upper portion of his chest. After visiting various physicians, the plaintiff finally consulted the defendant who recommended and then performed an operation to remove the particle. He was unable to locate it and it was not removed, but when the plaintiff awoke from the anesthetic his arm was numb and his hand useless. The sensory and motor paralysis in the plaintiff's arm became permanent.

One of the principal issues on appeal involved the admissibility in evidence of the testimony of one of the plaintiff's expert witnesses, Dr. Walker. After practicing general medicine in North Carolina for a number of years he took postgraduate courses in radiology and had engaged in that specialty for some nine years prior to the trial. He admitted that he had never done chest surgery and that in his general practice he had performed only minor operations. As a radiologist, however, he said that he came in contact with various types of surgeons in a consulting capacity, and he claimed to be acquainted with the generally approved practices among physicians and surgeons in North Carolina.

The trial judge, after full inquiry into Dr. Walker's education and experience, and with the opportunity and obvious disposition to appraise fairly the competency of the witness, permitted him to testify in respect to radiological matters. He allowed him to explain the uses of x-ray pictures, what they reveal, how they are employed by surgeons in determining the existence and location of foreign objects in the human body, and the correct interpretation of the roentgenograms made of the plaintiff. The judge did not, however, permit the witness to express opinions to the jury as to what constitutes proper surgical procedure in preparing for or performing chest operations.

The plaintiff contended that the exclusion of this testimony was reversible error because, if admitted, it would be sufficient to establish the standards of good surgical practice and make out a prima facie case of their violation.

The court of appeals held that the trial judge acted within the limits of his allowable discretion. He did not disqualify Dr. Walker as a matter of law because he was not a specialist in surgery but because, after weighing the witness' professional background and qualifications, the conclusion was reached that he had not shown sufficient familiarity with the subject upon which he was being interrogated to entitle him to express the opinion called for. The general rule, said the court, is that the qualification of a witness to express an expert opinion should be left to the sound discretion of the trial judge.

Dr. Walker's testimony, however, when coupled with the testimony of other of the plaintiff's expert witnesses, was sufficient to take to the jury the question of whether or not the defendant had failed

to exercise due care in the operation, or to use his best judgment in advising it. The court of appeals accordingly held that the directed verdict at the close of the plaintiff's evidence was improper, and the judgment in favor of the defendant was reversed and a new trial ordered. *Hunt v. Bradshaw*, 251 F (2) 103 (1958).

Malpractice: Consent for Operation.—This was an action for damages resulting from the alleged unauthorized performance of an operation by the defendant physician. From a judgment for the defendant the plaintiff appealed to the Supreme Court of Minnesota.

The plaintiff consulted the defendant physician in connection with various urinary problems from which he was suffering. After an office examination the defendant suggested that the plaintiff should enter the hospital in order that cystoscopic examination could be made. The defendant told the plaintiff "that the purpose of his going into the hospital was for further investigation with a view to making a prostate operation if the further examination showed that that was indicated." After the examination the next day the defendant performed an operation on the prostate gland during the course of which he severed the plaintiff's spermatic cords. The question was whether or not the consent to the prostate operation carried with it a consent to the severance of the spermatic cords.

The defendant testified that following the cystoscopic examination he went to the head of the table and talked to the plaintiff. He told him that a transurethral prostatic resection should be done and the plaintiff consented thereto. He admitted that he did not discuss any involvement of the spermatic cords although he did testify that severance of the spermatic cords is a routine part of this procedure in patients of the plaintiff's age. The plaintiff stated definitely that the defendant at no time told him that he was going to sever the spermatic cords. He admitted giving consent to the operation but insisted that the only thing he had in mind was his bladder because that was the reason for his consulting the defendant in the first place. The plaintiff also admitted, however, that he did not ask the defendant what he was going to do but left it up to him to do the right thing.

The general rule, said the Supreme Court, seems to be well established that before a physician may perform an operation on a patient he must obtain the consent either of the patient, if competent to give it, or of someone legally authorized to give it for him, unless an immediate operation is necessary to save the patient's life or health. In our opinion, the court continued, where a physician can ascertain in advance of an operation alternative situations, and no immediate emergency exists, a patient should be informed of the alternative possibilities and given a chance to decide before the doctor proceeds with the operation. In a situation such as the case before us, where no immediate emergency exists, a patient should be informed before the operation that if his spermatic cords were severed it would result in his sterilization, but that if this were not done there would be a possibility of an infection which could result in serious consequences. Whether the plaintiff's consent was obtained was a question which should have been submitted to the jury. Accordingly, the judgment in favor of the defendant was reversed and the cause remanded for a new trial. *Bang v. Chas. T. Miller Hospital*, 88 N.W. (2) 186 (Minn., 1958).

Lie Detector: Admissibility in Evidence of Results of Test.—This was a prosecution for rape and from a conviction in the trial court the accused appealed to the district court of appeal, first district, division I, California.

During the direct examination of the defendant by his own attorney, the defendant indicated that the only time he had been out of his cell on a particular day was when he had been given a lie detector test which he had volunteered to take. On cross-examination the prosecutor went more fully into the subject of the lie detector, discovered that the defendant did not know the results of the test which had been made, and offered such results in evidence. The defendant's attorney objected to this tactic, and the court instructed the jury that the lie detector test had no place in the case and that they should disregard any reference to it. During the closing arguments the prosecutor again referred to the matter. On appeal the defendant contended that the conduct of the prosecutor constituted reversible error.

The court said there was no doubt that evidence concerning the results of the lie detector test was inadmissible. Evidence of an accused's willingness or unwillingness to take such a test is also inadmissible. Generally, the admission of such evidence is error, and such error is not cured by a warning to the jury. There would seem to be little doubt that the defendant's statement that he had volunteered for and taken such a test was inadmissible. Had the prosecution objected the objection should have been sustained, but the prosecution did not

object; instead, on cross examination, it inquired into the subject more fully and even offered to introduce in evidence the result of the test.

In so proceeding, said the court of appeals, the prosecutor undoubtedly committed error. The law is clear that legitimate cross-examination does not extend to matters improperly admitted on direct. Immaterial and irrelevant testimony cannot be brought before the jury under the pretense that it is legitimate cross-examination.

The court of appeals held, however, that since the jury had been amply warned of the law on the subject and since there was other strong evidence of defendant's guilt, the error committed in this case did not require a reversal of the judgment of conviction. *People v. Parrella*, 322 P(2) 83 (Calif., 1958).

MISCELLANY

CODE OF ETHICS FOR HOSPITALS

The American Hospital Association and the American College of Hospital Administrators have released a revised code of ethics for hospitals and hospital administrators. The new code supplants a code produced and adopted in 1939 by the two organizations.

The revised code of ethics follows:

1. Recognizing that the care of the sick is their first responsibility and a sacred trust, hospitals must at all times strive to provide the best possible care and treatment to all in need of hospitalization.

2. Hospitals, cognizant of their unique role of safeguarding the nation's health, should seek through compassionate and scientific care and health education to extend life, alleviate suffering, and improve the general health of the communities they serve.

3. Hospitals should maintain and promote harmonious relationships within the organization to insure the proper environment for the considerate and successful care and treatment of patients.

4. Hospitals should appreciate and respect individual religious practices and customs of the patient.

5. Hospitals, to the extent possible, should conduct educational projects, stimulate research, and encourage preventive health practices in the community.

6. Hospitals should cooperate with other hospitals, health and welfare agencies, governmental and private, and other recognized organizations interested in promoting the health of the nation.

7. Hospitals in reporting their work to the public should give a factual and objective interpretation of accomplishments and objectives without disparaging the work of other hospitals or related organizations.

Submitted by the Council on Medical Service.

8. Hospitals should actively support and encourage every effective method which will ease the financial burdens of illness.

9. Hospitals should be fair, honest, and impartial in all their business relationships.

10. Hospitals should be progressive in policies, personnel practices, and efforts to maintain up-to-date equipment, methods, and standards of performance.

The statement and revised principles of conduct for hospital administrators are as follows:

The hospital administrator's life is dedicated to the highest possible level of performance in the competent and humane hospital care of the sick, in health education in all its many phases, and in research conducted in the interest of hospitals and their patients. In pursuing these objectives the hospital administrator should be guided by the following principles.

1. He will not use his position or influence for selfish personal advantage or gain and will not disparage the work of his colleagues.

2. As the official representative of the hospital's governing body and often the hospital's spokesman in the community, his conduct will at all times be dignified and exemplary. His professional performance will be objective and fair, with the patient's best interest as the ultimate consideration.

3. In his relationships with personnel and staff he will be impartial, tolerant, fair, and interested in all reasonable means of promoting personnel morale and welfare consistent with the hospital's best interests and ability to provide them.

4. The administrator will encourage, assist, and teach others the principles and practice of hospital administration to end that future hospital administrators may be more adequately prepared.

5. The administrator will encourage and participate, to the extent possible, in a broad educational program to assure the health workers necessary to the hospital field.

6. He will contribute his interest, support, and leadership toward the general improvement of the community, with especial emphasis on health education and related causes. In so doing he will attempt to avoid involving his hospital in partisan political issues.

7. In his relationships with the medical staff of the hospital he will support that which is constructive, sound, and in the interest of good hospital professional practice; he will resist and oppose that which is, in his judgment, harmful, destructive, or unwise.

8. The administrator will seek constantly to improve his professional knowledge and skill and will accept counsel and guidance, particularly in fields and subjects with which he is not entirely familiar.

9. Recognizing that his is a position of public trust, he will, within the limitations imposed by good judgment, legal consideration, and his hospital charter respect the rights, privileges, and beliefs of others regardless of race, color, or creed. He will keep confidential whatever he may learn respecting the private affairs or character of patients and their families, physicians, and others with whom he is associated in the hospital. When his administrative duties bring him into conflict with any segment of society or belief, he will deal with the situation with the greatest consideration, courtesy, and respect for the individual that is possible, without ridicule or animosity.

10. He will exemplify the Golden Rule in thinking, action, and conduct.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Diagnosis of Amyloidosis by Renal Biopsy. W. W. Ward Jr. J. Kentucky M. A. **56**:1226-1228 (Dec.) 1958 [Louisville].

The author reports on a 45-year-old woman with suspected primary amyloidosis and on 3 men, between the ages of 31 and 60 years, with suspected secondary amyloidosis, in whom the diagnosis was first established by percutaneous renal biopsy. Microscopic examination of renal tissue would seem to be a useful and rewarding procedure to confirm the diagnosis of amyloidosis, especially in the presence of abnormal urinary findings. This is particularly true when the nephrotic syndrome exists as a result of renal amyloidosis, since in patients with this syndrome both tubular and extensive glomerular involvement may be present. There were no complications resulting from renal biopsy in the 4 patients.

Prognostic and Diagnostic Value of Serum Glutamic Oxaloacetic Transaminase in Suspected Cardiac Infarction. K. D. Keele, F. Goulden and M. J. D. Newman. Lancet **2**:1187-1189 (Dec. 6) 1958 [London].

The authors report on 129 patients with 135 attacks of retrosternal pain, in whom cardiac infarction was suspected when they were admitted "off the street" to the Ashford Hospital in Middlesex, England. Estimations of serum glutamic oxalacetic transaminase (SGO-T) activity showed that the SGO-T activity is almost always increased between 24 and 48 hours after a myocardial infarct. Of 75 attacks of retrosternal pain proved to be due to cardiac infarction at autopsy or by the appearance of diagnostic electrocardiographic changes, only 2 were associated with an SGO-T activity of less than 50 units during this period, i. e., less than 3% of false-negative results. The height of SGO-T at its peak 24 to 48 hours after the onset of anginal pain proved to be closely correlated with the immediate mortality and the occurrence of heart failure. In 8 of 9 patients in whom cardiac infarction was diagnosed, a reading of over 300 units was associated with early death, the one exception being a 30-year-old man; of 20 patients with SGO-T between 200 and 300 units, heart failure or drop of systolic pressure below 100 mm. Hg occurred in 8 (40%), and 5 (25%) died within one month; of 57 patients with SGO-T below 200 units, heart failure occurred in 13 (23%), and 3 (5%) died. A false-positive result was found in 7 of 104 patients with raised SGO-T in this series. Anginal pain at rest with an abnormal but nonspecific electrocardiogram and raised SGO-T was found to carry the same prognostic significance as electrocardiographically proved infarction.

Pneumonia. H. J. Ustvedt. Tidsskr. norske lægefor. **78**:1051-1055 (Nov. 1) 1958 (In Norwegian) [Oslo].

Pneumonia is a disease of the lungs due to a number of different infectious substances. The better prognosis for life today in pneumonia in younger and middle-aged persons is essentially due to the treatment, preeminently with antibiotics, although a general increase of resistance may have operated simultaneously. Pneumonia is a dangerous disease for infants, old persons, and persons with a chronic disease. The morbidity from pneumonia is thought not to have been so strongly reduced as the lethality. The two main groups of pneumonia are the bacterial pneumonias, usually influenced by antibiotics, and the pulmonary inflammations due to virus or assumed to be conditioned on virus infection, which apparently are not affected, or are but little affected, by antibiotics but which nevertheless mostly have a good prognosis. When the diagnosis of pneumonia has been made, treatment should be started at once. In 9 out of 10 cases of lobar pneumonia, pneumococci are present, and penicillin is the antibiotic to start with. If the picture is grave, there is increased likelihood of the presence of other bacteria, and streptomycin should also be given from the beginning. This can be expected to affect staphylococci, Klebsiella organisms, and Hemophilus influenzae. Routine bacteriological examination of the sputum in pneumonia is superfluous. It is far more important for treatment and prognosis to concentrate examination for other possible diseases which may be present. Only if the initial treatment fails and the disease continues to show moderate or considerable activity is bacteriological examination of the sputum advised. The penicillin-resistant staphy-

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lococci represent a problem rapidly increasing in significance. In countries such as England, where the staphylococcus problem is today more acute than in Norway, attention is increasingly directed to staphylococci as the cause of fulminant pneumonias, in part resistant to therapy and fatal.

Virus diseases which do not primarily attack the lungs may be complicated with pneumonia. Here the pneumonia will be mostly bacterial, and special attention must be paid to staphylococci. Of the virus diseases which primarily seem to attack the lungs, with pneumonia as a characteristic manifestation, probably only diseases due to the so-called psittacosis–lymphogranuloma venereum type are of practical importance. The so-called common cold virus appears to play a small part, if any, as the direct cause of pneumonia. A bronchial carcinoma sometimes manifests itself clinically by a complicating pneumonia. It is, therefore, important that pneumonias, especially in cigarette-smoking men, aged 40 to 50 years and over, be followed to complete resolution. Particularly in men, aged 45 or over, in urban areas, chronic or recurring bronchitis, with gradually diminishing respiratory reserve, is not uncommon. Such patients will show a lower resistance to pneumonia, and the value of prophylactic sulfonamide or antibiotic medication in the winter season might be investigated here.

Effect of Weight Loss on Blood Pressure. J. V. Salzano, R. V. Gunning, T. N. Mastopaulo and W. W. Tuttle. J. Am. Dietet. A. **34**:1309-1312 (Dec.) 1958 [Chicago].

The authors studied the effects of a supervised reducing regimen on resting arterial blood pressure in 12 women, between the ages of 22 and 37 years, who were 14 to 85% above average weight, and in 4 men, between the ages of 24 and 32 years, who were 21 to 39% over weight. Nutritionally adequate diets were prescribed for each person, designed to produce a decrease in body weight of about 2 lb. (0.9 kg.) per week. The data obtained from these 16 persons before, during, and after weight reduction seem to justify the following conclusions. During the time observations were made after weight reduction, 13 (81%) of the 16 persons showed a significant decrease in systolic pressure, and 10 (62%) had a significant decrease in diastolic pressure. In 8 persons the systolic pressure was significantly reduced during the zero to 50% weight-loss phase, but during the reduction of the body weight to normal (50 to 100% excess weight-loss phase), 14 persons had a systolic pressure below their control values determined at the beginning of the study. Diastolic pressures were significantly less than control values during the zero to 50% excess weight-loss phase in 9 persons, but with the reduction of the body weight to normal, diastolic pressures were decreased from control values in 12 (75%) of the persons. On the basis of mean differences, there was a lowering of both systolic and diastolic pressure as the weight-loss program progressed.

The Course of Primary Hypertension in the Young. G. A. Perera. Ann. Int. Med. **49**:1348-1350 (Dec.) 1958 [Lancaster, Pa.].

The 30 patients reviewed were selected from the records of the Presbyterian Hospital in New York. Hypertension had been established in all of them before they reached the age of 25 years, and continued follow-up studies had revealed diastolic blood pressure values of 90 mm. Hg or higher. There were 11 male and 19 female patients. The average age at the time of diagnosis was 20 years. The ages ranged from 10 through 24 years, 5 patients being 15 years of age or younger. The initial recorded blood pressure ranged from 140/90 to 200/140 mm. Hg, and bore no relationship to the subsequent course. The diastolic blood pressure at the time of diagnosis was 120 mm. Hg or higher in 7 of the group. Eight patients (3 men and 5 women) died after a mean survival period of 21 years; the duration of the disorder in the cases followed until death varied from 10 to as long as 40 years. The accelerated ("malignant") form of hypertension developed in 4 of these and was demonstrated at autopsy. Three patients died of a cerebral hemorrhage, and in one the cause of death could not be determined.

The 22 patients who are still alive have been followed for an average period of 20 years. Seven of 8 patients who have so far survived for more than 20 years are women. Five of the 22 survivors have had cardiac pain or signs and symptoms of congestive failure; 1 has had a cerebral vascular accident; 6 now have proteinuria, and 3 have recently been found to have regional hemorrhages. The remainder, save for cardiac hypertrophy in the majority, are free of demonstrable organic complications. Half of those who are still living complain frequently of headaches, nervousness, palpitation, or dizziness; the rest have no subjective symptoms. These findings do not support the view that hypertension is necessarily more severe when it is contracted in youth.

Rheumatic Disease and Uric Acid Blood Content. L. Schiavetti, A. Gospodinoff and A. Violanti. Policlinico (sez. prat.) **65**:1725-1731 (Nov. 10) 1958 (In Italian) [Rome].

Uricacidemia was studied in 147 rheumatic patients, 32 with peripheral or vertebral rheumatoid involvement, 22 with gouty arthropathy, 66 with arthrosis, 8 with rheumatic fever, 6 with syndrome of the intervertebral disk, 6 with secondary rheumatic infection, and 7 with other forms of rheumatic disease, such as fibrositis and scapulohumeral

periarthritis. The group of patients with peripheral or vertebral rheumatoid involvement was composed of 20 women and 12 men. In the women, all between the ages of 40 and 55 years, on a normal diet the average value of uric acid content in the blood was 2.3 mg. per 100 cc.; only in one of them did this content reach 3.1 mg. per 100 cc. On a 10-day low-purine diet the average value of the uric acid content was 1.6 mg. per 100 cc., while with a high-protein diet the average value of the uric acid content was 2.9 mg. per 100 cc. The highest value of blood uric acid on a normal diet was 8.12 mg. per 100 cc.; on a low-protein diet this value diminished markedly and reached an average value. The average uric acid blood level in the men, all between the ages of 45 and 55 years, was 2.3 mg. per 100 cc. on a normal diet; only in one patient was this value as high as 6.2 mg. per 100 cc., and it became normal on a low-protein diet. Normal values of blood uric acid were found in 4 patients with vertebral rheumatoid involvement; changes occurring in these values proved to be independent of the diet. Considerable increase in the erythrocyte sedimentation rate occurred and was found to be in direct relationship with the clinical symptoms. No relationship was found between the erythrocyte sedimentation rate and the values of uric acid in the blood. Treatment with a proprietary preparation of isoniazid (Pyrizidin) and with prednisone had some good effect on the clinical symptoms and on the sedimentation rate, but had no effect on the uric acid blood content.

Of the 22 patients with gouty arthropathy, 14 were men and 8 were women. The men were between the ages of 41 and 65 years. On a normal diet the average value of blood uric acid was 6.8 mg. per 100 cc., and the minimum value was 5.6 mg. per 100 cc.; after 10 days of a low-purine diet the average value was 4.7 mg. per 100 cc.; on a rich purine diet the average value was 9.2 mg. per 100 cc., with a maximum value of 16.5 mg. per 100 cc. and a minimum value of 6.8 mg. per 100 cc. In the women, all between the ages of 50 and 70 years, the average value of blood uric acid on a normal diet was 5.9 mg. per 100 cc., with a minimum value of 4.7 mg. per 100 cc.; on a low-purine diet the average value was 4.5 mg. per 100 cc., and on a high-purine diet it was 8.6 mg. per 100 cc., with a maximum value of 12 mg. per 100 cc. Treatment with synthetic steroids had a marked effect on the uric acid blood level. Values lower than normal were found in the uricacidemia of the patients with rheumatoid disease, with the exception of patients with vertebral forms of rheumatism in whom marked oscillations were observed. High uric acid blood level was found in patients with arthrosis. A decrease in the values of uric acid and an improvement in the painful symptoms resulted from the administration of drugs favoring uricaciduria in patients with arthrosis and hyperuricacidemia.

Study of 1000 Cases of Asthma and Rhinitis. F. Grégoire and M. Comeau. Canad. M. A. J. **79**:981-985 (Dec. 15) 1958 [Toronto].

The authors studied 679 patients with bronchial asthma, 230 with perennial rhinitis, and 289 with hay fever, representing about 55% of the 2,200 patients seen in 5 years at the Lavoisier Institute in Montreal. The majority of these patients were followed up and were hyposensitized by the family physician. These patients were asked to report on details about their medication and hyposensitization and to appraise the degree of improvement after discussion with the family physician.

Results showed that 78% of all the patients with bronchial asthma registered moderate improvement to complete remission, while the condition of 10% of the asthmatics was unchanged, especially that of the older age group, and another 12% showed only slight improvement. Functional tests on hospitalized patients showed that irreversible emphysema was one of the causes for lack of response. It is, therefore, suggested that patients with asthma be treated as early as possible and before irreversible emphysema develops. Almost 90% of the patients with perennial rhinitis and 95.5% of those with seasonal rhinitis (hay fever) showed improvement, most of them very substantially. This improvement rate could be increased further by better education of the patient and his family physician. Prophylaxis with antibiotics could be tried in infected patients, as is done in patients with rheumatic heart disease, but with antibiotics other than penicillin, because the latter might have a dangerous effect in allergic patients. Hyposensitization should be continued for at least 3 years and should not be stopped if the patient has had a recurrence of his symptoms in the last 2 years or if his skin tests are still strongly positive.

The Diagnosis of Gout: Significance of an Elevated Serum Uric Acid Value. J. C. Goldthswait, C. F. Butler and J. S. Stillman. New England J. Med. **259**:1095-1099 (Dec. 4) 1958 [Boston].

In the period from 1949 to 1956, 225 patients whose serum uric acid levels were higher than 6 mg. per 100 cc. were studied and classified for diagnosis. The Archibald modification of the Kern-Stransky method was used for determination of the serum uric acid content. Seventy-eight of the 225 patients gave a classic history of gout: acute attacks of arthritis with symptom-free intervals between attacks. In 26 patients a diagnosis of gout was made, although the course of the disease as well as symptoms and physical abnormalities were not characteristic of gout; in each patient at least one criterion for the establishment of this diagnosis was fulfilled in addition to the presence of hyperuricacidemia. Thirty-two of the 225 patients had rheumatoid arthritis, and it was predominantly associated with

hyperuricacidemia in the 22 men. The initial serum uric acid levels were not as high in patients with rheumatoid arthritis (mean, 6.6 mg., and ranging from 3.4 to 9.7 mg. per 100 cc.) as in those with gout (mean, 7.8 mg., and ranging from 4.8 to 16.0 mg. per 100 cc.). Roentgenologic examinations of the hands and feet of 26 patients showed in 4 patients "punched-out" lesions in the bones of these areas. Twenty-three patients were classified in the category of atypical rheumatoid arthritis.

Twelve patients in this series of 225 had psoriasis. The disease of the joints in 3 consisted of acute episodic symptoms which responded well to colchicine administration; therefore, these patients were classified in the group with gout. The condition of one patient was diagnosed as atypical gout; although the physical symptoms were typical, the history (6 months of subacute pain and swelling in the ankles and toes) and the reaction to therapy were not typical of gout. Eight patients were considered to have rheumatoid arthritis. Forty-seven patients were classified as having diseases unrelated to gout or rheumatoid arthritis. Thus, of the total group of 225 patients with hyperuricacidemia, the diagnosis of gout was made in 113. The remaining 112 patients either presented some well-defined entity other than gout or rheumatoid arthritis, or the findings were not susceptible to a diagnostic label. Hematocrit determinations were made on 109 patients; the hematocrit reading was higher than 45% in 33, and this was associated with persistent leukocytosis in only 1 patient. Splenomegaly was not found in any of these patients. Neoplastic diseases of the bone marrow, such as leukemia or myeloma, were not found in any patient of this series.

Some Observations on the Management of Thyroid Disease. W. A. Seldon. M. J. Australia **2**:637-638 (Nov. 8) 1958 [Sydney].

A survey was made of the previous therapy received by 507 patients with goiter seen at a private clinic during the years 1956-1957. This number did not include patients with carcinoma of the thyroid or thyroiditis. The definitive diagnosis was nontoxic goiter in 377 of the patients, and the remaining 130 were thyrotoxic. The number of patients receiving "thyroid-affecting" drugs was 129 (or 25%). Patients were placed in this category if they had received iodine, iodides, or thyroid extract within 2 months prior to being seen, or if they had taken antithyroid drugs, chiefly Neomercazole or methylthiouracil, within 3 months before they attended.

It has been recognized since the inception of radioiodine (I^{131}) uptake testing that previous iodine medication will interfere with normal uptake by the gland. The time taken for this effect to wear off depends on the iodine dosage, the length of time it has been administered, and the degree of activity of the gland. Experience has also shown that overdosage with antithyroid drugs in normal or thyrotoxic subjects will cause a falsely high result from the I^{131} uptake test. This test and the estimation of serum protein-bound iodine are the sheet-anchors of laboratory investigation of thyroid disease. The estimation of serum protein-bound iodine is a difficult technical procedure which can be done only in specially equipped laboratories. With modern techniques of measurement of gland uptake of I^{131}, a clear-cut separation of hyperthyroid, euthyroid, and hypothyroid subjects can be obtained.

Of the 130 patients whose condition was finally diagnosed as thyrotoxic, 49 (31%) were receiving antithyroid drugs when first seen. In some cases this did not matter, as the disease was florid and the diagnosis obvious. However, in a number of instances it was impossible to decide whether the patient had well-controlled thyrotoxicosis or whether one was dealing with an euthyroid patient who had been given antithyroid therapy with resultant compensatory hyperplasia of the gland. In the latter case the thyroid enlarges and develops a bruit from increased vascularity, so that it is indistinguishable from the goiter of Graves's disease. Of the 377 patients with nontoxic goiter, 34 (9%) were receiving antithyroid drugs. This was due to the presence of a coincidental anxiety state, which produced symptoms superficially resembling thyrotoxicosis. This diagnostic error is easily made but could be avoided simply by the use of uptake tests before instituting therapy. An estimation of the basal metabolic rate is of no value in these instances, as it usually gives a high result.

In the treatment of nontoxic goiter, thyroid extract and thyroxin are the quickest and most efficient drugs, and yet they had been given to only 3% of the patients. If care were taken to give enough of these drugs to suppress iodine uptake by the gland, the author never failed to obtain decrease of the goiter within 6 months. Even nodular goiters will diminish in size with this therapy. With such an effective form of treatment available, there is no reason for persisting with iodine therapy in nontoxic goiters, and its use should be abandoned.

Buccal Mucosal Tests in Patients with Canker Sores (Aphthous Stomatitis). L. Tuft and L. S. Girsh. J. Allergy **29**:502-510 (Nov.-Dec.) 1958 [St. Louis].

Recurrent canker sores (aphthous stomatitis) are common in children and young adults, but their etiology is not known. Allergic etiology has been considered but has not been proved. There is general agreement, however, that excessive ingestion of such foods as citrus fruits, melons, tomatoes, vinegar, wine, chocolate, and nuts (walnuts) seems to play a role in the formation of the ulcers. Other

suggested etiologies include (1) avitaminosis, since improvement at times follows vitamin B or vitamin C therapy, and (2) bacterial infections, since diplococci and streptococci are found in cultures from the lesions. The canker-sore lesions begin as small, single or multiple, yellow-gray papulovesicles, 2 or 3 mm. in size. These lesions are quite sensitive. Within a few hours they change into tender ulcerations, which is the way they usually appear by the time they are inspected. The sites most often involved include the buccal mucosa, the edges of the tongue, the gingivae, and the palate. The oral lesions appear in successive crops at irregular intervals. They heal without scarring in a week or two. In 1956 Tuft and Ettleson reported the results of a clinical study of an allergic patient who had recurrent canker sores of the mouth for many years. They were able to reproduce these ulcers by direct application of citric acid and acetic acid to the buccal mucosa, and thus they proved the etiological relationship of these agents to the canker sores. Their results prompted further investigations into the possibility of utilizing this method of testing as an aid in etiological diagnosis not only in patients with canker sores but perhaps also in those with other forms of allergy to food or drugs.

The authors describe studies on patients with recurrent canker sores. Various methods were tried, and the following method was evolved. The authors placed 0.5 cm. of testing material, if crystalline (as in the case of citric acid and tartaric acid), or a 0.5-cm. cotton pledget saturated with the liquid organic acid (as in the case of acetic acid, vinegar, or lactic acid) on the anterior buccal mucosa on either side of the frenulum of the lips and as far laterally (1 cm.) from the frenulum of the lower lip as possible in order that 2 tests could be done at one time. The test material was removed at the end of 3 minutes. Only 4 organic acids, citric, acetic, tartaric, and lactic, were tested, since these are commonly found in foods. Citric and tartaric acids were tested in powder form. Acetic acid was tested as a 5% solution or as vinegar. Lactic acid was tested as 0.1 *N* solution (pH 2.4), which approximates the concentrations usually used in food recipes.

The test was found diagnostically useful in patients subject to recurrent canker sores. The condition was reproducible in 6 of the 46 patients with canker sores tested with citric acid and in 4 of the 35 patients tested with acetic acid. Tartaric acid and lactic acid gave negative tests and were not considered of etiological importance. A history of canker sores was much more frequent in allergic patients than in nonallergic control patients. None of the nonallergic patients in the control group had a positive reaction, that is, a canker sore as a result of the test. The utilization of this method of testing in the diagnosis of food allergy in skin-test-negative patients and in drug allergy is indicated.

Hepatitis and Cirrhosis in Women with Positive Clot Tests for Lupus Erythematosus. L. G. Bartholomew, A. B. Hagedorn, J. C. Cain and A. H. Baggenstoss. New England J. Med. 259:947-956 (Nov. 13) 1958 [Boston].

Lupus erythematosus has rarely been regarded as a potential etiological factor in patients presenting prolonged jaundice. The purpose of this study is to describe a group of women who presented not only prolonged jaundice with evidence of grave impairment of the liver but also hypergammaglobulinemia, L. E.-cell phenomenon, and clinical evidence of diffuse lupus erythematosus. The 7 women were observed at the Mayo Clinic. Scrutiny of their clinical histories indicated a disease of multiple systems and of long duration. The involvement of the liver, although a major manifestation, invariably occurred late in the course of the illness. Four of the 7 women were less than 25 years of age. Early in the course of the disease, episodic and migratory joint manifestations, including pain, swelling, and redness, were prominent in 5 of the 7 patients. Three of these 5 patients had joint symptoms so severe that prolonged steroid therapy was required, and a 4th patient had been treated with phenylbutazone. The remaining 2 patients had a history of significant arthralgia. Recurring episodes of unexplained fever had been recorded in 6 of the patients. Typical pleuritic pain was noted in the history of 4 patients. Repeated examinations of the urine in 6 of the 7 cases demonstrated the sporadic occurrence of albuminuria, microscopic hematuria, and cylindruria. Five of the 7 patients manifested either a definite sensitivity to sunlight or an unusual susceptibility to drugs. Intermittent, transient erythematosus or urticarial eruptions were noted in 3 patients during an exacerbation of joint pains. Four of the 7 patients had more than the usual amount of acne. All 7 patients had anemia. For periods varying from a few months to several years, episodes of unexplained weakness and excessive fatigability had occurred in all these women. These patients had been under medical management for these various manifestations for periods ranging from 6 months to 13 years. It was the recent development of jaundice or some other evidence of hepatic decompensation that seemed to precipitate the terminal phase in those who died of their systemic illness.

For varying periods before the evidence of hepatic disease appeared, these patients presented protean symptoms consistent with the clinical diagnosis of disseminated lupus erythematosus. At the time when objective evidence of grave disease of the liver was evident, they presented, in general, the unusual clinical picture of apparent well-being, strikingly different from that ordinarily expected in other forms of serious disease of the liver. The outstanding laboratory findings included marked

hypergammaglobulinemia, positive serologic reaction for syphilis, extreme elevation of the sedimentation rate, and abnormal urinary sediment. Among the tests of hepatic function that gave unequivocally abnormal results were the thymol turbidity and cephalin-cholesterol flocculation tests and the determinations of serum albumin, prothrombin time, and serum bilirubin. The typical cells of disseminated lupus erythematosus were repeatedly demonstrated in the serum or bone marrow in every case. In the cases in which the authors were able to examine the liver histologically, the lesion resembled that of acute and subacute viral hepatitis in 3 cases and postnecrotic cirrhosis in 2 cases.

Pneumonia Complicating Asian Influenza. N. C. Oswald, R. A. Shooter and M. P. Curwen. Brit. M. J. **2**:1305-1311 (Nov. 29) 1958 [London].

The clinical and pathological records and roentgenograms of 165 patients with pneumonia complicating influenza, admitted to the 10 London undergraduate teaching hospitals in the autumn of 1957, were reviewed. Of these, 20 (12%) were instances of staphylococcic pneumonia. In order to compare staphylococcic and nonstaphylococcic pneumonia, the 20 patients with staphylococcic pneumonia were extracted from the teaching hospital series and added to those from nonteaching hospitals, so that comparison was possible between 145 cases of nonstaphylococcic pneumonia from teaching hospitals and 155 cases of staphylococcic pneumonia from a large number of hospitals in and near London. The serious consequences of secondary infection by Staphylococcus pyogenes var. aureus was proved by the fact that there were 44 deaths (28%) among the 155 patients with staphylococcic pneumonia, and 18 deaths (12%) among the 145 patients with nonstaphylococcic pneumonia. The clinical features also confirmed the virulent nature of staphylococcic pneumonia. Compared with nonstaphylococcic pneumonia, it caused a severer and longer illness, with a higher and more prolonged fever, roentgenologic evidence of more extensive pulmonary involvement, and, most important of all, a high mortality among children and young adults.

Experience during this epidemic left the question of the choice of antibiotics for routine use to some extent unsolved. The majority of patients overcame their pneumonia uneventfully, and penicillin and tetracycline appeared to be equally effective. The problem lay with the 10 to 15% of patients in whom staphylococcic pneumonia developed. Patients treated at home in the first instance, as were one-third in this series, may reasonably be given penicillin or tetracycline in the knowledge that it is suitable for nonstaphylococcic infections, and will rapidly resolve about one-half of the staphylococcic infections. Once patients have been admitted to hospital, close cooperation with the laboratory is necessary, so that staphylococci may be identified and their sensitivities reported. This system was in use in many hospitals taking part in this investigation, and accounts partly for the frequent changes in antibiotic therapy within 48 hours of admission in the staphylococcic series. Many of the patients had features which are associated with a grave prognosis, such as mental changes, prostration, pallor, cyanosis, and excessive dyspnea. In a number of instances the influenza was superimposed upon other diseases—for example, chronic bronchitis and cardiovascular disorders.

In order to enlarge the experience of these more formidable aspects, a further 79 cases of nonstaphylococcic pneumonia were added to the staphylococcic and nonstaphylococcic groups compared above, making 379 cases altogether. Some of the additional 79 cases were thought originally to be instances of staphylococcic pneumonia and represented a selected group with severe infections. A diagnosis of fulminating influenza is often made in patients whose clinical features are alarming and in whom toxemia is extreme. Perhaps the outstanding qualities of fulminating influenza are the short duration of the acute illness and the severe degree of toxemia, so that effective treatment to combat collapse must be given quickly. In addition to oxygen therapy, administration of antibacterial drugs, and the maintenance of a clear airway, the possibility of steroid therapy arises, the value of which in the present epidemic produced conflicting opinions. There were 27 patients who received steroid therapy in adequate dosage, usually 100 mg. of hydrocortisone intravenously, followed by 50 mg. at 6-or-12-hour intervals; of these, 17 died. The relative importance of obstructed airway, loss of effective alveolar surface, and toxemia could not be accurately assessed. Also, 8 of the deaths occurred within 24 hours of admission to hospital. However, the impression is that the survivors were those with a reasonably free airway and comparatively little roentgenologic evidence of consolidation. These responded promptly to a combination of hydrocortisone and antibiotics.

Intermediary Ammonia Metabolism During Hepatic Coma: Significance of Blood Ammonia Determination as an Aid for Diagnosis and Management of Patients with Cirrhosis. C. S. Lieber and A. Lefévre. Acta clin. belg. **13**:328-357 (July-Aug.) 1958 (In French) [Brussels].

The level of serum ammonia in the arterial and venous blood was determined by means of modified Conway method with 180 blood samples obtained from 7 patients with hepatic cirrhosis, from 16 patients with various other diseases, and from a control group consisting of 7 healthy persons. In

cirrhotic patients with impending coma or in actual hepatic coma, the ammonia level of the arterial blood was found to be significantly higher than that of the venous blood. According to these findings, the ammonia level of the arterial blood correlated better with the degree of psychic disturbances than did the ammonia level of the venous blood. The blood ammonia level remained almost normal in patients who were in comatose state due to other diseases (uremia, cerebral thrombosis), and there was no significant difference between the average arterial and the average venous blood ammonia levels in normal persons. Moreover, there was no change in the condition of cirrhotic patients in whom the levels of arterial and venous blood ammonia were measured before and after complete removal of the ascitic fluid, and there was no rise in ammoniemia in any of these patients after the latter procedure. It was detected, however, that the concentration of ammonia in the ascitic fluid was entirely different from that in the peripheral venous blood.

The significance of the difference between the ammonia level of the arterial blood and that of the venous blood and the pathogenesis of hepatic coma associated with disturbances in intermediary ammonia metabolism are discussed. The authors stress the importance of blood ammonia determination in that it offers differential diagnosis of a coma of hepatic origin from a coma of nonhepatic origin and, furthermore, makes it possible to adjust the protein intake to the individual tolerance of each cirrhotic patient. Restriction of protein ingestion not only is useful as a preventive treatment for impending coma and actual hepatic coma but also causes improvement in more chronic psychic disturbances sometimes occurring in patients with severe cirrhosis. The low-protein diet and the administration of antibiotics, however, do not prevent the occurrence of complications usually associated with cirrhosis, the most frequent being gastrointestinal hemorrhage.

Lucerne as a Cause of Respiratory Allergy in South Africa. D. Ordman. South African M. J. **32**:1121-1122 (Nov. 22) 1958 [Cape Town].

Lucerne, a perennial legume, is one of the principal crops in the Union of South Africa and is grown almost exclusively for hay. It is a good source of protein and mineral matter and is used as a feed for all classes of livestock, for which purpose it is often ground to meal. Lucerne may cause vasomotor rhinitis and bronchial asthma, especially when it is handled in the dry state during baling of the hay or when it is milled into powder. In the farming districts of the Orange Free State, where lucerne respiratory allergy is not uncommon, it has been observed that children, mainly boys, 5 to 10 years of age, develop mild urticaria after helping in the lucerne fields. In 1952 the realization that allergic sensitivity to the inhalation of lucerne dust was of significance stimulated a close study of each case that subsequently came to notice. Information about the patients was obtained largely by correspondence with the physicians concerned. In this way, from 1952 to 1957, reports were received of 38 patients with a clinical sensitivity to the inhalation of lucerne dust (confirmed by skin testing in 18 cases where this was done). In 23 patients the sensitivity was to lucerne alone, and in the other 15 there was a coexisting sensitivity to one or more cereals.

Among 24 lucerne-sensitive patients whose occupation could be ascertained, there were 16 farmers, 3 agricultural students working on farms, 3 workers in grain stores or mills, and 2 school children. Lucerne extracts were issued to physicians for desensitizing purposes in 30 treatment sets, either alone (19), together with a single cereal extract (6), or together with 2 or more cereal extracts (5). Details are given of 6 cases of lucerne sensitivity in patients with symptoms of respiratory allergy, in whom desensitization with lucerne extract was carried out and in whom the results of desensitization could be assessed. Specific desensitization in respiratory allergy due to the inhalation of lucerne dust is shown to be very satisfactory.

SURGERY

Direct-Vision Coronary Endarterectomy for Angina Pectoris. W. P. Longmire Jr., J. A. Cannon and A. A. Kattus. New England J. Med. **259**:993-999 (Nov. 20) 1958 [Boston].

The authors report on 5 men, between the ages of 38 and 54 years, who had suffered incapacitating anginal pain and underwent coronary endarterectomy under direct vision. All the patients had coronary atherosclerosis and typical symptoms of angina pectoris without definite evidence of myocardial infarction; they were selected for surgical intervention in the hope that the intact myocardium would tolerate the stress of operation better than an extensively damaged one and that maximal symptomatic improvement might be expected by an increase in the flow of blood to the undamaged myocardium. In all the patients it has been possible to remove an almost totally occluding, thickened intimal core from one or more of the main coronary vessels and to reestablish the blood flow through the vessels at the time of the operation. Asystole occurred near the completion of the operation in one patient who died despite vigorous application of all usual resuscitative measures. The 4 surviving patients, who were followed up for 2 or 3 months postoperatively, showed marked improvement in the electrocardiographic tracings which were obtained during a treadmill exercise test. Two

of the 4 patients have been completely relieved of their anginal pain, and the frequency and intensity of the anginal attacks have been greatly reduced in the other 2 patients. These results indicate that it is technically feasible by this surgical procedure to reestablish the blood flow in previously obstructed major coronary arteries. Experience with additional patients and longer postoperative follow-up will be necessary to make a final assessment of the value of the procedure.

The Surgical Correction of Calcific Aortic Stenosis in Adults: Results in the First 100 Consecutive Transaortic Valvuloplasties. D. E. Harken, H. Black, W. J. Taylor and others. J. Thoracic Surg. 36:759-776 (Dec.) 1958 [St. Louis].

The authors report on 71 men and 29 women, 38 of whom were between the ages of 51 and 66 years, who were operated on for symptomatic aortic stenosis. Surgical correction was carried out by a transaortic digital manipulation of the valve employing an Ivalon sponge operating tunnel. Of the 16 operative deaths, 5 occurred in the last 60 patients, representing a mortality rate of 8%. Of the 84 patients who survived the operation, 12 died within 1 to 31 months after the surgical intervention. Congestive heart failure was the predominant cause in 6 of these. Of the remaining 72 survivors, 50 have been followed for from 6 to 36 months; clinical appraisal of these 50 survivors indicates that the conditions of 43 (86%) are improved. Hemodynamic evaluation by left heart catheterization before and after the surgical intervention showed that the valve area has been significantly increased, that the mean systolic gradient has been reduced, and that the work performed by the left ventricle has been reduced. Serious consideration of surgical relief is advised in all patients with symptomatic aortic stenosis. A plea is made for careful preoperative and postoperative clinical and hemodynamic evaluation of patients with aortic obstruction. This should facilitate the proper choice of closed or open operation in the various patterns of disease.

Pulmonary Resection in the Treatment of Tuberculosis: Experience with 1,730 Patients. R. J. Barrett, H. S. Neal, J. C. Day and others. J. Thoracic Surg. 36:803-817 (Dec.) 1958 [St. Louis].

The authors performed 1,769 pulmonary resections on 1,730 patients with pulmonary tuberculosis at the Herman Kiefer Hospital in Detroit between Nov. 1, 1949, and Dec. 31, 1957. The current status is known in 91.4% of the patients. Detailed data have been presented on the last 1,567 resections performed on 1,528 patients. Of the 1,567 resections, 100 were pneumonectomies; 787, lobectomies; 579, segmental resections; and 101, wedge or local excisions. The operative mortality was 2.9% and the late mortality 1.9%—a total mortality rate from all causes of 4.8%. There is still active disease in 3.8%. The incidence of bronchopleural fistula was 6.2%. Relapse occurred in 83 patients, a total incidence of 5%. Four (4.8%) of the 83 patients died, and 51 (62%) still have active disease. The seriousness of positive sputum at the time of operation was reflected in a significantly higher morbidity and mortality rate. Despite this higher operative risk, the continued use of resection in patients with extensive disease, in whom the prognosis is otherwise grave, appears justified with due regard to the limitations imposed by lowered pulmonary function, emphysema, and advanced age. During the past year, 297 resections have been performed, with a total mortality of only 1.3%, or less than half the mortality rate of the entire series.

Surgical Treatment of Thirty-five Cases of Drainage of Pulmonary Veins to the Right Side of the Heart. H. T. Bahnson, F. C. Spencer and C. A. Neill. J. Thoracic Surg. 36:777-802 (Dec.) 1958 [St. Louis].

The authors report on 35 patients, between the ages of 3 months and 45 years, with anomalous pulmonary venous return, in 16 of whom all the pulmonary veins drained to the right side. These patients, who underwent surgical treatment for their cardiac defects, represent 38% of the 92 patients treated during the past 9 years for left-to-right shunt at the atrial level. Partial anomalous drainage into the right atrium can be readily treated with modification of the techniques used in repair of the simple atrial septal defects. For this the authors used hypothermia, inflow occlusion, and suture under direct vision and were satisfied with this method in treating 10 patients, in 1 of whom all pulmonary veins entered the right atrium. Of 15 patients with drainage into the right superior vena cava, the latter vessel was partitioned in 11 to direct the pulmonary venous blood to the left side through the atrial defect, which then was closed under direct vision with the aid of inflow occlusion and hypothermia. All the patients treated by this method obtained a good result.

Cardiopulmonary bypass was used in treating successfully 2 patients with total pulmonary drainage into the coronary sinus. The third patient with this anomaly, an infant who was operated on with the aid of hypothermia, died, partly because the correct diagnosis was not made before death. In the remaining 7 patients, all pulmonary veins entered the left superior vena cava. Anastomosis of the left interior pulmonary vein to the atrial appendage was performed on 1 patient, anastomosis of the left atrial appendage to the venous trunk was performed on 2, an aortic graft was used to join the left atrium and venous trunk in 1, and transposition of the right superior vena cava to the

foramen ovale was attempted in 1; all these patients died. Cardiopulmonary bypass was used to treat the last 2 patients, an infant and an adult with pulmonary drainage into the left superior vena cava; the infant died, but the adult obtained a good result. In patients with total pulmonary drainage into the coronary sinus or into the left superior vena cava, cardiopulmonary bypass is considered essential to allow adequate time for exploration and treatment, a conclusion supported by the poor results obtained with other methods used in earlier cases.

Seven Years' Experience with Transventricular Aortic Commissurotomy. R. P. Glover and H. L. Gadboys. J. Thoracic Surg. 36:839-856 (Dec.) 1958 [St. Louis].

The authors report on 78 patients, between the ages of 4 and 57 years, with aortic stenosis, who were operated on at the Presbyterian Hospital in Philadelphia between 1951 and 1957. Seventy of the 78 patients had moderate to marked calcification of the aortic valve, and 13 had permanent atrial fibrillation. The first 37 patients were operated on with the aid of a now outmoded technique employing a large, three-bladed, expandable split-dilator inserted through a widely purse-stringed avascular area near the apex of the left ventricle; 17 of the 37 patients died, representing an operative mortality of 46%. The remaining 41 patients had split-dilatation of the aortic valve by a greatly refined method with use of a light but exceptionally strong dilator, the expandable head of which was equipped with 2 parallel blades, rather than 3 as were formerly used; 2 of the 41 patients died, representing an operative mortality of 4.9%. The average systolic peak gradient across the valve was reduced from 78 mm. Hg to 27 mm. Hg. There were 15 late deaths, 8 in the earlier group and 7 in the group operated on by the present operative technique. Thirty-four patients (12 of the 37 operated on by the older technique and 22 of the 41 operated on by the new technique), who had survived the operation for more than one year, were definitely improved by it. Until the diseased aortic valve can be totally removed and replaced, the transventricular approach seems to offer the best form of surgical palliation with the least possible risk.

Hydatid Cyst of Posterior Aspect of the Left Ventricle: Pathologic Q Wave. R. Di Bello, R. Rimini and A. Roca Estevez. An. Fac. med. Montevideo 43:59-66 (May-Aug.) 1958 (In Spanish) [Montevideo, Uruguay].

Hydatid cyst of the heart is more frequent than is believed. Rupture of the cyst in the heart causes massive passage into the blood of allergens from the cystic material, with consequent severe anaphylactic reactions, implantation of multiple visceral metastases, and arterial embolization. Rupture of the cyst into the pericardium causes secondary pericardial hydatidosis, with consequent pressure upon the atriums and upon the large blood vessels and the same severe allergic, metastatic, and embolic phenomena as those caused by the primary cyst. A woman, 60 years old, complained of pain in the left hemithorax of 4 months' duration. There was no history of cardiac disease in the patient's family. Roentgen-ray examination of the chest showed deformation of the shadow of the lower border of the left heart and pathological shadows on the left ventricle and the lower cardiophrenic angle. Abnormalities of the electrocardiogram included the characteristic inverted T coronary wave and a pathological Q wave in the leads which corresponded to the locations of the hydatid cyst. At operation a cyst was noted on the posterior surface of the ventricle, as well as symphysis of the pericardium and calcification of the pericardial serosa. These were interpreted as signs of rupture of the hydatid cyst 4 months before the operation, when local pain started. The operation consisted of evacuation of the cyst, resection of the cystic wall, and antihydatid toilet of the involved region of the ventricular wall. A drainage was left in situ for 40 days. The postoperative period was uneventful. A follow-up over a 2-year period has shown that the patient is in satisfactory condition.

Thoracic Fibromas. H. Hilke and R. M. Konrad. Arch. klin. Chir. 290:48-63 (no. 1) 1958 (In German) [Berlin].

Among the benign tumors of the thorax, the fibrous neoplasms have a special status as regards origin, classification, and potential malignancy. The authors discuss thoracic fibromas on the basis of observations on 11 patients with these tumors observed at the clinic of the Medical Academy of Düsseldorf, Germany. They found records of 166 intrathoracic fibromas (including their own) in the literature available to them. Intrathoracic fibromas may originate from the connective tissue of the thoracic wall, from the mediastinum or its organs, from the supporting tissue of the lungs, and from the connective tissue of the bronchial wall, but fibromas develop most frequently from the visceral or the parietal pleura. In the case of the small fibrous tumors classification as regards origin causes little difficulty, and if these tumors have pedicles with a profuse blood supply, their origin can likewise be readily ascertained. Pedicle formation is particularly characteristic of the intrathoracic fibromas that originate from visceral or parietal pleura on the thoracic wall, but it has also been observed in fibromas that originate from the mediastinal side of the sternum or from the pericardium.

Eight of the 11 thoracic fibromas observed by the authors were pleural fibromas. The histological findings in these 8 cases are presented. Two of the remaining 3 patients had mediastinal fibromas, and 1 had endobronchial fibroma.

The symptomatology of thoracic fibromas is largely identical with that of other benign intrathoracic tumors. A definite preoperative diagnosis is possible only in the case of the endobronchial fibromas, because here exploratory biopsy is possible. The treatment should be surgical, not only because of the possibility of malignant degeneration but also because these tumors may interfere with vital functions by causing displacement of mediastinal organs. The prognosis after radical extirpation of the tumor is favorable, but recurrences have been reported. In 5 of the 8 reported cases of pleural fibroma in which follow-up studies were carried out as late as 8 years after the operation, no recurrences were observed.

The authors point out that American investigators have suggested that a pleural fibroma (circumscribed fibrous mesothelioma) should be differentiated from other intrathoracic fibromas because of a characteristic pleomorphism. The authors feel that they cannot accept this stand because the 8 pleural fibromas they observed showed the typical structures of benign fibromas. Of the 166 intrathoracic fibromas reviewed, 68 were on the visceral pleura, 24 on the parietal pleura, 50 in the mediastinum, 14 in the thoracic wall, and 10 in the lung.

Radical Small-Bowel Resection: Report of Two Cases. R. H. Jordan Jr., J. R. Stuart and J. D. Briggs. Am. J. Digest. Dis. 3:823-843 (Nov.) 1958 [New York].

Available evidence suggests that resection of 50 to 60% of man's small intestine is compatible with a normal existence; however, the surgeon may have to resect more than that amount. At such times the question arises, What degree of disability may be expected by patients who survive operation? The purpose of this paper is to evaluate by a review of the literature the postoperative status of patients surviving radical resection (75% or more) of the mesenteric small intestine and to report 2 new cases. Forty-four cases reported in the literature fulfilled the criteria for radical small intestine resection and were observed for a minimum of 3 months after operation. To this series the authors add the case of a patient who survived 2½ years in good health with only 35 cm. of small intestine remaining. Evaluation of the postoperative results in these 45 patients revealed that excellent or good results were obtained in all but 10 of the patients, that is, 35 of the patients were not incapacitated. Although the study of these cases did not conclusively indicate the relative importance of the jejunum and the ileum for maintenance of nutrition, the results appeared best when a portion of the ileum, rather than a segment of the jejunum, remained. Since no patient lived longer than 10 months after duodenocolostomy, it appears that a segment of mesenteric small intestine is essential for life and that the only indication for retaining intestine of questionable viability is the avoidance of total excision of the small intestine. Early operation for necrotic intestine is important, not only to reduce postoperative mortality but also to increase the likelihood of a viable segment of small intestine.

Occasionally the necessity for radical resection of the small intestine and subtotal gastrectomy occurs in the same patient. Since either procedure alone may produce serious nutritional problems, it was not unexpected that both operations on the same patient would yield poor clinical results. The authors found reports of 8 cases with both procedures in the literature, and they add the history of a 9th patient. The results were excellent in 2 patients, who had 4 to 5 ft. of remaining small intestine, good in 1, and poor in 6. It is suggested that the gastrointestinal continuity in patients surviving this combination of operations be restored by a gastroduodenostomy. By this procedure 20 to 40 cm. of intestine, bypassed by other types of anastamoses, is made available for digestion and absorption. The data summarized suggest that the response to radical resection of the small intestine is variable and cannot be closely correlated with the age or sex of the patient and the length of the remaining intestine. Satisfactory results after resections in this category depend in part upon the patient's psychological motivation and in part upon continuous careful management of his diet and health, particularly during periods of stress.

Acute Gastric and Duodenal Ulcers After Thoracic Surgical Interventions. F. Rotthoff, R. M. Konrad and K. H. Willmann. Arch. klin. Chir. 290:31-38 (no. 1) 1958 (In German) [Berlin].

At the Surgical Clinic of Düsseldorf, Germany, the authors observed 20 patients in whom acute gastric or duodenal ulcers or erosive hemorrhages developed immediately after operations on thoracic organs, such as the heart, the large vessels, or the lungs. Since formerly the authors had not been in the habit of resorting to roentgenologic examinations when patients complained of discomfort in the abdominal region after thoracic operations, they believe that the aforementioned 20 cases do not include all such cases that occurred at their hospital. In 5 of the 20 patients massive hemorrhages occurred, of which 3 were fatal. In 2 others the hemorrhages were threatening, but they could be arrested by conservative methods. In the remaining patients there existed more or less severe gastrointestinal symptoms, with occult blood in the

stools or roentgenologically demonstrable ulcers of the stomach or duodenum. The ages of the 20 patients ranged from 4 to 65 years.

The signs and symptoms appear suddenly and without premonitory symptoms in the severe forms or after a history of typical disturbances. The duration of the operation, the type or depth of anesthesia, and the age and sex of the patient appear to have no influence on the development of the acute peptic ulcerations. In some patients with threatening hemorrhages, the authors were unable to detect roentgenologic signs of ulcers, whereas in patients who had practically no symptoms they sometimes found definite niche formation on the roentgenograms. Nearly all the patients had a gastritis characterized by hypersecretion. For this reason the authors believe that a hemorrhagic gastritis might have existed in the patients in whom ulcers could not be detected roentgenologically. In autopsy studies they discovered in 2 cases erosive changes in the mucosa of the stomach as well as of the duodenum. The older theories on the pathogenesis of these ulcerations suggested neurogenous processes by way of the hypothalamus and the vagal nerves. Selye showed that so-called stress processes may induce acute gastrointestinal ulcers during the shock phase. More recent investigations, however, demand a humoral component that acts by way of the hypothalamus, the hypophysis, and the adrenals. The authors at present are conducting routine investigations on the acid values of the stomach during thoracic operations carried out with the patients under intratracheal anesthesia. They observed a considerable hypersecretion in all cases but feel that definite conclusions are not as yet justified.

On Portacaval Anastomosis in Patients with Cirrhosis: Case Reports. A. Vannotti. Helvet. med. acta **25**:298-301 (Oct.) 1958 (In French) [Basel, Switzerland].

The author presents 6 cases observed in the medical clinic of the University of Lausanne, in which the clinical picture of hepatic cirrhosis was accompanied by frequent hemorrhages of the digestive tract, resulting from large esophageal varices, and by the appearance of ascites, distended abdomen, and a strongly developed venous network on the abdominal wall. Portacaval anastomosis considerably improved the clinical picture of these patients, and all of them were able to return to work. The author makes suggestions as to the cause of circulatory disturbances in the veins of cirrhotics. One of them is that there may be a vasodilating substance in the blood which would normally be destroyed but is no longer metabolized by the impaired liver. Besides peripheral vasodilatation due to such a vasodilating substance and to increase in volume of circulating blood, there is probably in the cirrhotic a vasodilatation due to loss in elasticity of the perivascular structures.

In all the cirrhotic patients who underwent portacaval anastomosis, liver function, as measured by bilirubin and urea levels, by prothrombin, flocculation, and Bromsulphalein tests, and by esterification of cholesterol, remained practically unchanged. Circulatory disorders, though, were favorably influenced by this operation which avoided portal hypertension and its grave consequences—hemorrhage and ascites. Portal hypertension generally provokes splenic stasis and frequently splenomegaly, and, in general, there is no regression of signs of hypersplenism when portal hypertension and splenic stasis have been eliminated by portacaval anastomosis. Splenic reticulosis also causes splenic stasis. It is frequently useful to combine a splenectomy and a portacaval anastomosis in a two-stage operation. Cirrhotics who have large esophageal varices, and especially those who have had serious hematemeses in the past but whose tests show that liver function is still relatively efficient, are good operative risks. The Bromsulphalein test should not reveal more than 25% retention one-half hour after injection; the total level of serum albumin should not be lower than 3.5 Gm. per 100 cc.; the level of serum bilirubin should not be above 1 mg. per 100 cc.; and the prothrombin concentration should not be below 50%.

The great danger present in cirrhosis is gastroesophageal hemorrhage, with its indirect consequences in anemia and hypoproteinemia and its effect on circulatory and hepatic functions. Research at Lausanne on the subject of enzymatic activity of the hepatic parenchyma has shown that 12 different enzymes are active in liver. In hepatic cirrhosis, the activity of a series of enzymes regulating the reduction in carbohydrates and the Krebs cycle is clearly diminished, and oxidative phosphorylation is measurably inhibited. These studies show that apoferment especially is insufficient in hepatic cirrhosis.

Management of Patients with Massive Resection of the Small Intestine with Special Reference to the Use of Steroid Hormones. E. Kogan, A. Schapira, H. Janowitz and D. Adlersberg. Am. J. Digest. Dis. 3:844-856 (Nov.) 1958 [New York].

In an earlier communication the authors reported clinical observations on 11 patients who had undergone massive resection of the small intestine. In this paper they discuss difficulties and problems involved in the management of these patients. The chief symptoms after intestinal resection of great magnitude are anorexia, diarrhea, and steatorrhea. Loss of weight may be considerable. Proper diet is one of the cornerstones of therapy and should be high in carbohydrates, preferably monosaccharides,

moderately high in protein, and low in fats. Replacement of deficits in minerals, vitamins, and fluid is difficult. It requires flexibility of approach and careful observation of the symptoms and signs presented by each patient. The results vary with the patient and depend on the magnitude of the resection and complications, such as tetany, hemorrhagic manifestations, and changes in the skeleton.

The results obtained with the use of steroids in the primary malabsorption syndrome (nontropical sprue) prompted their trial in 2 patients who had undergone massive resection of the small intestine and in whom conventional therapy failed. These 2 patients as well as a third, reported elsewhere, are presented to illustrate the problems that occur in the management of this condition. Adrenocortical hormones cause a definite, often dramatic clinical improvement in patients resistant to the accepted forms of therapy. It is suggested that corticotropin (ACTH) or steroids be used when malabsorption appears in the postoperative period after sacrifice of significant areas of small intestine. Later, therapy should be continued with smaller maintenance doses of corticosteroids, preferably prednisone or prednisolone.

NEUROLOGY & PSYCHIATRY

Early and Late Manifestations of Closed Craniocerebral Injuries in the Electroencephalogram. F. Pampus. Chirurg **29**:484-487 (Nov.) 1958 (In German) [Berlin].

While the changes and deviations from the normal in the electroencephalographic curves permit deductions about type, extent, and localization of brain lesions, the diagnostic value of electroencephalographic studies is restricted in several respects. For instance, the leads are taken not from the brain but from the scalp, thereby isolating delicate fluctuations in electrical potential. The media interposed between cerebral cortex and the recording electrodes, such as the subarachnoid fluid, the dura, the bone, the galea, and the skin, produce physical scatter, so that small zones with reduced electrical activity are covered by the rhythms of adjoining regions, whereas circumscribed foci with increased electrical activity are registered encephalographically far beyond their site of origin. Furthermore, the electrical discharges of the cerebral cortex are manifestations of vital functions that are determined not only by cerebral functions but also by disturbances in the circulation and in the oxygen, carbon dioxide, and sugar contents of the blood and by the acid-base equilibrium.

The electroencephalographic changes like the clinical manifestations are influenced by the time at which they are recorded and by the severity of the injury. The author, who was able to make electroencephalographic studies on boxers within a few minutes after relatively mild trauma, found that deviations from normal activity are relatively frequent, but subside within a few hours or days and do not recur. In patients with more severe injuries, the electroencephalographic changes disappear more slowly, or even increase in severity during the first few days, not only in intensity but also in extent. These "secondary" increases must be interpreted as sequels of reactive processes in the damaged region, being caused by vasospastic reactions or by pathological metabolic processes, and may lead to an activation in the cerebral potential and to dysrhythmias that may reach spasmodic potentials. They are frequently followed by a retardation in the basic rhythm. Delta waves of less than 4 per second always indicate cerebral edema. The clinical picture of these patients often indicates an organic brain lesion, by the secondary appearance of neurological focal signs or by serious disturbances in the general condition. Prolonged systemic disturbances are a sequel either of lesions deep in the brain stem or of an inflammatory cortical irritation. This latter condition may be caused by hemorrhage from subarachnoid contusions and the post-traumatic meningeal reaction, or by a progressive infectious meningitis. Massive, progressive focal symptoms suggest an intracranial hemorrhage or an early abscess.

The author also calls attention to observations he made during the secondary post-traumatic phase in boxers. In those with disturbances of consciousness, he observed systemic changes that persisted for the entire period of anterograde amnesia. In one boxer with secondary loss of consciousness that followed a relatively mild punch to the head, the sequels of progressive circulatory damage could be demonstrated microscopically in the form of extensive necroses of the brain stem. There seems to be only a difference in degree between temporary and irreversible manifestations. A secondary circulatory impairment or hypoxia of the brain may transform primary reversible lesions into irreversible tissue changes, that is, into necroses of the ganglionic cells.

These secondary changes may be caused by local factors, such as vasovasal reflexes, cerebral edema, or spasmodic action of the brain. On the other hand, on the basis of brain-stem-induced disturbances in the central regulations, conditions of shock or collapse may lead to an inadequate blood perfusion. Furthermore, by an increase in body temperature or by spasmodic attacks, the metabolic and blood requirements of the brain may become increased, so that the normal blood supply becomes inadequate and tissue gangrene results. The author concludes that a normal electroencephalogram, especially if only one record is taken, cannot rule out an organic brain lesion but that, if electroencephalographic records are made early and re-

peatedly during the first week after the trauma, they will provide valuable supplementary information about the sequels of closed craniocerebral injuries. Although alone electroencephalographic studies are insufficient, they help to clarify clinical and neurological findings that may suggest multiple diagnostic interpretations.

An Approach to the Problem of Homosexuality in the Military Service. L. J. West, W. T. Doidge and R. L. Williams. Am. J. Psychiat. 115:392-401 (Nov.) 1958 [Baltimore].

The Armed Forces of the United States do not accept a homosexual, and during the last 5 years governmental policies concerning homosexuality have become much more punitive. Special military regulations have placed more emphasis on the necessity for identifying and disposing of the homosexual person. After citing some of the existing regulations, the authors review their studies on homosexuality at a large Air Force psychiatry clinic during the 4-year period from 1952 to 1956 when 458 military personnel (16% females) were examined for homosexuality. In 75% of these cases no diagnosis was made, and a routine certificate was prepared, indicating that the subject had been found able to distinguish right from wrong and to adhere to the right, able intelligently to cooperate in any proceedings concerning him, and in sufficiently good mental health that a medical discharge was not in order. Of this group some were persons who had confessed a homosexual act or who had been apprehended in such an act. Many were not true homosexuals. A good number had been named as suspects, but there was no real evidence. Retention was urged in 69 cases in which a psychiatric recommendation to this effect might be needed to resolve the issue. A diagnosis of character and behavior disorder was made in nearly 19% of the cases; two-thirds of the acts of this group were immaturity reactions. Many of these individuals were recommended for general discharge, in the belief that their homosexual acts did not indicate a sexual perversion but rather were minor by-products of emotional immaturity.

A representative group of 201 homosexuals have been followed. About 75% received an undesirable discharge, although the psychiatrist had recommended retention of many of these persons. The final dispositions of 25% were as follows: retained in the service, 16.4%; general discharge, 5%; other administrative discharges, 2%; resignations (officers), 1.5%; and medical discharge, 0.5%. The procedures employed by the Air Force in processing each case were time-consuming, requiring from 1 to 15 months or an average of 5 months. During this period the accused was usually on "casual status," in a special barracks with assorted sexual and other offenders awaiting separation from the service. These persons were assigned to work-details but were almost never permitted to continue their regular duties.

One hundred fifty individuals, including all referrals for homosexuality, were carefully examined by a team of psychologists, a psychiatric social worker, and a psychiatrist. Most of the gross psychopathological conditions were concentrated in the 25% who were exclusively or predominantly homosexual. Their diagnosis usually was severe psychoneurosis or character disorder. They all obtained significantly pathological scores on most of the psychological tests. The remaining 75% (predominantly heterosexual persons) did not deviate significantly from a control group of airmen awaiting separation for various administrative reasons, and deviated only slightly from a group of healthy controls who had no gross adaptational difficulties. Many of the 75% were deemed good candidates for retention in the service; others seemed to deserve no worse than a general discharge, as unsuitable because of immaturity. The suggestions offered by the authors for a new approach to the problem of homosexuality in the military service include (1) modification of punitive official attitudes, (2) elimination of routine extensive investigations, (3) establishment of the primary disorder as the basis for discharge, (4) elimination of the special stigma, (5) utilization of benign investigation procedures, and (6) fulfillment of present potentially liberal retention policies.

Mepacrine Therapy for Children with Petit Mal. R. A. Miller. Scottish M. J. 3:441-444 (Nov.) 1958 [Glasgow].

Since literature reports indicated that the administration of quinacrine (mepacrine) benefits patients with petit mal epilepsy but that the condition tends to become worse when treatment is stopped, the administration of a smaller dose over an indefinite period was tried in the hope that patients might not have a relapse when treatment was terminated. Sixteen children, between the ages of 5 and 12 years, were selected for the investigation. All had suffered from petit mal attacks for periods ranging from 4 months to 4 years. All had been given Tridione for at least 2 months, and most had received courses of other anticonvulsive drugs. As soon as quinacrine therapy was started, all previous forms of treatment were terminated. The 16 children treated were given 100 mg. of quinacrine daily from Monday to Friday of each week for 3 to 24 months. After this period, 10 patients still had symptoms sufficiently severe to justify a modification of their treatment, and 9 of these were given meprobamate (Miltown) as well as quinacrine, the dose of Miltown being 200 to 400 mg. each day in addition to 100 mg. of quinacrine 5 days in each week. After 1 or 2 months of this treatment Miltown was replaced by Tridione in 5 of

these 9 children, the dose being 0.3 Gm. given 2 or 3 times a day, depending upon the patient's age and the incidence of the fits. The course of the combined therapy was 3 to 7 months.

In 15 of the 16 children treated, the parents had gained the impression that quinacrine was better than any of the other preparations the patients had received. Six of the children became asymptomatic, and in 9 the symptoms were less marked. When these 9 were given an anticonvulsive drug in addition to quinacrine, they improved still further. Their petit mal attacks were trivial and did not occur more than twice a day. This had not been possible when anticonvulsive drugs were given alone. Treatment with quinacrine resulted in a marked reduction of akinetic attacks in one patient and cessation of psychomotor attacks in another. Tridione, on the other hand, had no appreciable beneficial effect upon either of these patients. The value of Tridione was enhanced in 5 children by giving it together with quinacrine. In a 6th patient Tridione was more effective after a course of quinacrine than before it. Two difficulties were encountered: one was the production of skin pigmentation by quinacrine, and the other was the occurrence of grand mal attacks in 2 patients. In one, the beneficial effect of quinacrine therapy was doubtful, so the drug was withheld. Though the other patient had improved during the administration of quinacrine, the treatment was curtailed. Little is known of the effect of quinacrine on grand mal attacks.

GYNECOLOGY & OBSTETRICS

Intravascular Gas in the Radiological Diagnosis of Foetal Death in Utero. P. Ross. M. J. Australia **2**:495-497 (Oct. 11) 1958 [Sydney].

While the diagnosis of fetal death in utero can usually be suggested on clinical grounds, most authorities agree that roentgenologic examination is indicated for confirmation. The demonstration of signs of maceration, particularly in the skull and spine, are generally regarded as significant. This paper emphasizes the importance of detecting gas in the fetal circulatory system, a sign which was first described by Roberts in 1944, and which since 1949 has been reported by a number of other investigators. The author says that altogether 48 cases have been recorded up to the present time. Gas has been shown in the vessels of the head and neck, the heart and lungs, the abdomen, the extremities, and the umbilical cord. However, the most characteristic appearances are the rounded, lobulated shadows made by gas in the heart and the tree-like shadow of gas in the vessels of the liver. The common sites of gas in the dead fetus are the heart and the vessels of the abdomen, and only rarely is gas seen elsewhere when it is not demonstrable in these regions.

The case of a 37-year-old woman is presented. The patient stated that fetal movements had ceased 4 days previously. Roentgenologic examination revealed a single fetus of about 38 weeks. There was no misalignment or overlapping of the skull bones. The upper thoracic spine showed a little accentuation of its curvature. In the lateral film of the abdomen, a large collection of gas was seen within the heart, and the aorta, great vessels of the neck, and upper abdominal vessels were clearly outlined. The diagnosis of fetal death was made, and a dead, macerated female infant was delivered.

From 65 to 75% of fetal deaths in utero will exhibit roentgenologic signs when such examination is first requested. The roentgenologic signs do not appear within the first 48 hours after fetal death. Evidence has now accumulated to suggest that gas in the fetal circulatory system is the most important roentgenologic sign of death in utero. 1. The presence of gas in the fetal circulation is an absolutely certain indication of fetal death. 2. Gas can be unequivocally detected by roentgenologic examination before the onset of labor in at least 80% of the cases in which it is present. 3. Gas occurs about as frequently in cases of fetal death in utero as definite signs of maceration do, that is, each occurs in about 50% of all cases, probably independently of the other. 4. Gas usually appears earlier than the signs of maceration, often about 3 or 4 days after fetal death; the origin of the gas is unknown. It is recommended that a recumbent anteroposterior view and an erect lateral view be taken routinely in all cases of suspected fetal death in utero.

Latent Genital Tuberculosis in Women, Its Early Diagnosis and Treatment. I. Halbrecht. Tuberkulosearzt **12**:712-716 (Nov.) 1958 (In German) [Stuttgart, Germany].

Whereas formerly tuberculosis of the female genitalia was regarded as a rare disease with a serious prognosis, it is now known to be generally asymptomatic and comparatively frequent. In the last 15 years, and in several countries simultaneously, latent tuberculosis of the female genitalia is being accepted as a new clinical form, the chief complication of which is sterility. Most investigators agree that this genital tuberculosis is in most cases secondary to primary pulmonary tuberculosis. About the time of the menarche, occasionally earlier, or between the ages of 15 and 20 years, the tuberculous infection is carried by the blood to the genitalia. It is not clear, though, why the uterine tubes, and not simultaneously also the endometrium, become first involved. It likewise has not been explained why cervical tuberculosis is rather frequent in some and rare in other countries.

The author and his associates at the women's clinic of the Hasharon Hospital in Petah Tiqua,

Israel, began in 1944 to make cultures of the menstrual blood and of the intermenstrual cervicovaginal excretions in order to detect genital tuberculosis. Curettage and/or these culture methods have been used at the author's clinic in 600 patients, in 113 of whom tuberculosis of the genitalia was either detected or corroborated. In 40 patients cultures of the menstrual blood were the only diagnostic method used, curettage seeming to be contraindicated since these women either had inflammatory tumors of the pelvis or were virgins; the suspected presence of genital tuberculosis was confirmed in 25 of the 40 patients. In 48 cases cultures and curettage gave identical positive results. In the remaining 40 cases cultures yielded positive results, whereas curettage of the endometrium did not reveal tuberculosis; it is assumed that these were isolated forms of tuberculosis. There were also 13 cases in which biopsy revealed tuberculous endometritis, while cultures were negative.

The author believes that a minimum of 6 to 8 consecutive negative cultures are necessary to exclude genital tuberculosis, and in rare cases a positive result was obtained even after 9 or 10 negative cultures. This is the only method that insures an early diagnosis so essential for the efficacy of antibiotic therapy. Triple antibiotic therapy with streptomycin, isoniazid, and aminosalicylic acid produced cure in 80% of the patients without a recurrence over a period of 4 years. Unfortunately cure of genital tuberculosis rarely signifies cure of sterility. Of the 31 pregnancies that resulted after cure, 21 were extrauterine pregnancies, and 5 others terminated in abortion. The author believes that by analogy it is logical to attribute to spontaneously cured latent genital tuberculosis many of the extragenital pregnancies that are observed in general practice.

PEDIATRICS

The Use of Chromatin Sex Determinations in the Assessment of Fertility and Intersex Infants. J. A. Epstein, D. K. Briggs and H. S. Kupperman. Fertil. & Steril. 9:521-532 (Nov.-Dec.) 1958 [New York].

The morphologic distinctions of the various somatic cells assign a person to one or the other chromatin sex, the normal male being referred to as "chromatin negative" and the female as "chromatin positive." The essential difference between chromatin-positive cells and chromatin-negative cells is that in the former there is an extra chromatin mass associated with the nucleus. Sex diagnosis from the oral mucosal smear and skin biopsy is based on the difference in the number of cells showing the extra chromatin mass associated with the nucleus. In the male less than 4% of the cells show this piece of chromatin, whereas in the female more than 20% show it. In the blood smear, a single chromatin mass ("drumstick") on the polymorphonuclear neutrophils indicates a chromatin-positive person. There is no drumstick in a normal male; the diagnosis of a male or chromatin-negative person depends not on a low number of chromatin masses but on their absolute absence. Since many persons were found, both normal and abnormal, with as few as 1 or 2 drumsticks to every 500 cells, it is quite possible that a blood smear can be taken from one of these persons, 500 cells examined, and no drumsticks found. This might lead to a mistaken diagnosis of genetic male. However, by paying attention to the nonstalked masses of chromatin, to which Davidson and Smith gave the name of "sessile nodules," the authors found that a preliminary examination of 500 cells gives the important clue to sex diagnosis, by revealing either some sessile nodules or some drumsticks in chromatin-positive patients.

The authors report on 4 patients, 2 adults and 2 infants, in whom this technique of chromatin sex determination was used and in whom the chromatin sex studies were of value in guiding clinical management and assessing the reproductive potential. One of the adults was a 34-year-old man with a history of azoospermia of 9 years' duration. Libido was adequate. The patient shaved daily and had normal male distribution of hair. There was moderate bilateral true and false gynecomastia with some hyperpigmentation of the areolas. The penis was normal in size; both testes were unusually small, and the prostate was poorly developed. A diagnosis of gonadal dysgenesis (Klinefelter's syndrome) was made. On the basis of a positive chromatin pattern and the associated findings, further attempts at unraveling the infertility problem in this patient were believed unwarranted. The second adult patient was a 24-year-old woman with primary amenorrhea and absent secondary sex characteristics, in whom a diagnosis of gonadal dysgenesis (Turner's syndrome) had been made. Her chromatin sex pattern was negative. The patient responded to cyclic estrogen and progesterone therapy with development of secondary sex characteristics. The advantage of the chromatin sex determinations in this patient was not only to emphasize the futility of any aspirations for fertility but also to make the physician aware of the need for appropriate substitution therapy in such a patient in order to achieve adequate development of secondary sex characteristics.

Cases of intersex were presented by the 2 infants, aged 3 weeks and 7 months respectively. The finding of a positive chromatin pattern in the 3-week-old infant was of considerable help, along with 17-ketesteroid-excretion studies, in substantiating the diagnosis of pseudohermaphroditism due to adrenal hyperplasia. In the older infant with no significant history other than the indeterminate sex

organs (with a small phallic structure and an empty, poorly developed scrotal sac) noted since birth, the female chromatin sex pattern proved to be of inestimable value in deciding the eventual sexual and social behavior of the infant. In view of the unlikelihood of the patient's ever having a functional phallus or of being a fertile male, it was felt that the positive chromatin pattern, together with the clinical status, directed the management of this child toward assuming a feminine role in society. Once the chromatin sex has been determined, it is possible to tell the parents whether the patient is likely to be fertile in the chosen anatomic sex. Thus, if the female sex has been chosen for an infant, but the chromatin sex study shows that the child is chromatin-negative, it can be stated categorically that the child will be sterile.

A Staphylococcus Type-80 Epidemic in a Maternity Hospital Illustrating Some Special Features. M. C. Timbury, T. S. Wilson, J. G. P. Hutchison and A. D. T. Govan. Lancet 2:1081-1084 (Nov. 22) 1958 [London].

The authors report an outbreak of infection due to Staphylococcus pyogenes var. aureus which occurred among infants in the Royal Maternity Hospital in Glasgow. The exceptionally virulent phage-type 80 of Staph. pyogenes var. aureus was first isolated on Nov. 19, 1957, from a submandibular abscess in a baby transferred to the sick-nursery from one of the units of the maternity hospital in which the infants normally stayed beside their mothers' beds in the postnatal wards. Thereafter, until the hospital was closed 6 weeks later, on Jan. 4, 1958, the phage-type 80 strain caused 14 of the 18 infections appearing in the sick-nursery. During the epidemic period the incidence of all staphylococcic infections among the infants was 11%; the figure for infection due to type 80 was 8%. The infections were serious in 9 of the 18 infected infants, and all the serious infections were due to type 80. Five of the 9 babies who had serious infections died. A total of 8 deaths were associated with the epidemic.

When the hospital was closed, nasal swabs were taken from 475 members of the medical, nursing, administrative, and domestic staffs; 38% were found to carry Staph. pyogenes var. aureus in the nose, but only 3 persons (0.6%) harbored the epidemic strain. Staph. pyogenes var. aureus was isolated from many samples obtained from dust from floors, curtains, screens, blankets, furniture, and equipment, but type 80 was found once only. Thus, the nasal carriage rate of type 80 among the staff and the rate of colonization of the hospital environment were remarkably low. Of 99 babies who were discharged from the hospital when it was closed, infections developed shortly afterward at home in 21 (21%). Only 4 of these infections caused by staphylococci acquired in the hospital were due to type 80. This was in striking contrast to the distinct predominance of type 80 in infections in the hospital, but was in accord with the type-80 nasal carriage rate found among infants in the hospital. Ten of the 12 strains other than type 80 which were isolated were penicillin-resistant, indicating that they too were probably acquired in the hospital. This finding suggests that, even in the absence of the epidemic strain, hospital-acquired staphylococci would still be giving rise to a considerable amount of infection. Babies known to have carried or to have been infected with type 80 were visited 4 months after discharge from hospital. There was no indication that the epidemic strain tended to persist unduly in the noses of these children.

Follow-up surveys are essential to determine the true extent of staphylococcic infection acquired in maternity hospitals. Serious staphylococcic infection appearing among infants after discharge should be reported to the local health authority and the hospital in which they were born. In attempting to solve the problem of infection in maternity hospitals, one of the first necessary steps is to discover by systematic inquiry into individual outbreaks the full extent of neonatal hospital-acquiring staphylococcic disease as well as the phage-type and the possible source of the infection.

INDUSTRIAL MEDICINE

Industrial Thallium Intoxication. E. M. Richeson. Indust. Med. 27:607-619 (Dec.) 1958 [Chicago].

The author reports on 15 men who were employed by an Ohio plant engaged in the separation of industrial diamonds from abrasives. One step in the process depended on differential separation of the diamonds from certain minerals by gravity in varying concentrations of solutions of organic thallium salts. All but 3 of the men had complaints which may have resulted from their exposure to the organic thallium salts for periods up to 7½ years. A diagnosis of thallium intoxication was eventually made in 6. The chief complaints were abdominal pain, fatigue, weight loss, pain in the legs, and nervous irritability. A diagnosis of appendicitis was originally made in 3 of the men, and 2 of them were subjected to surgical treatment. Albuminuria occurred in 3 patients, and hematuria in 1. One patient had abnormal results from the liver function test, and elevated cerebrospinal glucose and protein levels were observed in one patient. The blood pressure of a 22-year-old man was elevated during his hospitalization for an appendectomy but returned to normal within one month. He returned to work with thallium for another 3 years; during the last 8 months his blood pressure remained elevated and after 4 years in another occupation

was still abnormally high. He had, however, a history of having had on a single occasion a slightly elevated blood pressure before his first exposure to thallium.

Thallium intoxication can present diagnostic difficulties, especially if the history does not reveal any contact with the metal. This is true in early cases of chronic poisoning, because subjective symptoms are not necessarily accompanied by clinical signs or positive laboratory findings. There is no adequate information on certain laboratory tests to ascertain which would be the most useful aids in establishing a differential diagnosis. Urinary excretion of thallium is rare in unexposed persons, but no relationship between excretion rate and either exposure or the appearance of symptoms has been established. Two of the patients with thallium intoxication were treated with dimercaprol (BAL); this agent did not effect prompt relief of symptoms in these 2 patients and apparently did not materially alter the urinary excretion rate in the patient from whom such data were available.

Cancer of the Lung and Nose in Nickel Workers. R. Doll. Brit. J. Indust. Med. **15**:217-223 (Oct.) 1958 [London].

In 1949 the Minister of Pensions and National Insurance of Great Britain classified cancer of the lung and cancer of the nose as industrial diseases when they occurred among certain classes of workers engaged in the refining of nickel. Data were collected from the records of deaths in districts in which workers at a nickel refinery lived. From the ratio of deaths attributed to lung cancer to deaths from causes other than cancer of the lung and nose among the other men resident in the same area, an estimate was made of the number of lung cancer deaths which would be expected to have occurred among men employed in 4 specified occupational groups. During the years 1948-1956, there were 139 deaths from "other causes" among nickel workers and 48 from lung cancer; the expected number of lung cancer deaths among them was 9.9. The excess did not appear to be due to a bias in favor of diagnosing lung cancer among nickel workers, and it is concluded that during 1948-1956 the risk of nickel workers dying of the disease was approximately 5 times "normal."

During 1948-1956, 13 deaths among nickel workers were due to cancer of the nose. An estimate based upon the national mortality data suggested that the expected number of deaths was less than 0.1 and that the nickel workers' risk of dying of the disease was approximately 150 times "normal." Comparison of the data for 1938-1947 with those for 1948-1956 provided no evidence of any substantial change in the annual number of deaths due to these specific diseases. There was, however, an increase in the average age at which death occurred, and no excess in mortality was apparent for those under 50 years of age. It is, therefore, reasonable to believe that the hazard has been largely or completely removed in the last 35 years. The total number of deaths which are now known to have occurred among British nickel workers from cancer of the lung and nose are, respectively, 126 and 62.

THERAPEUTICS

Preliminary Observations on the Treatment of Postirradiation Hematopoietic Depression in Man by the Infusion of Stored Autogenous Bone Marrow. N. B. Kurnick, A. Montano, J. C. Gerdes and B. H. Feder. Ann. Int. Med. **49**:973-986 (Nov.) 1958 [Lancaster, Pa.].

The authors report on 2 men, aged 36 and 62 years, with carcinoma of the testes and with renal carcinoma associated with pulmonary metastases, in whom irradiation therapy was proposed and whose diagnostic bone marrow aspirates revealed no infiltration. Before the institution of roentgenotherapy, bone marrow was collected from the sternum and iliac crests and preserved by freezing with the aid of the Polge technique. The cells were stored in a dry-ice chest for periods varying from 14 days to 2 months, during which the patients received roentgenotherapy to the entire torso. The stored diluted bone marrow specimens, which revealed about 80% of the cells to be viable, were infused intravenously after the irradiation. Serial bone marrow examinations revealed severely hypoplastic marrow at the end of roentgenotherapy, followed by progressive increase in active centers in both patients on the 3 occasions of marrow infusion after roentgenotherapy, the first patient receiving 2 such infusions. Since on rare occasions spontaneous recovery from hematopoietic depression may occur, it cannot be concluded that the response in the hematological picture in these 2 patients was due to the infusion of the autogenous bone marrow. It can, however, be said with certainty that the infusion of the bone marrow was innocuous and did not interfere with rapid bone marrow recovery, and that it may have been responsible for it.

The storage in a viable state of bone marrow permits reinfusion of autogenous marrow after hematopoietic depression, which has occurred after irradiation therapy in patients who are to undergo extensive roentgenotherapy. No problem of immunological reaction, such as occurs with homologous transplants, is concerned. The method has particular application for patients with potentially curable malignancies requiring extensive, rapid roentgen-ray irradiation. Such patients are often deprived of adequate therapy because of the hematopoietic depression. The authors felt encouraged

to continue the bone marrow infusion method, and in an addendum they report on 2 additional patients who were given infusions of stored autogenous bone marrow. The results showed repopulation of the bone marrow within 2 to 4 weeks. A group of patients who had less severe bone marrow depression were followed without reinfusion of their stored bone marrows. Serial bone marrow aspirates in these patients revealed persistent hypoplasia 2 to 9 months after completion of the irradiation therapy.

Experience with Reserpine (Serpasil) and Perphenazine (Trilafon) in Acute Alcoholic Intoxications and Alcoholic Psychosis. O. Kofman. Canad. M. A. J. **79**:988-991 (Dec. 15) 1958 [Toronto].

The author reports experiences in the treatment of 163 alcoholic patients in the acute stage who were given reserpine (Serpasil) and 114 others who were treated with perphenazine (Trilafon), an amino derivative of chlorphenothiazine, during 1955-1958 in the Toronto General Hospital. As a control series, the effects of treatment of the reserpine-treated group were compared with a group of 500 patients previously treated under similar circumstances with intravenously administered insulin and dextrose. On admission, the patients in the first group received 2.5 mg. of reserpine intramuscularly. A further 2.5 mg. was given in 1 hour and again routinely in 6 hours if the patient was still restless. Further amounts were used if the patient remained unsettled. After this, the patient was given either 0.25 or 0.50 mg. of reserpine by mouth 4 times each day. None of the patients with delirium tremens treated in this manner retained their hallucinations beyond a 36-hour period; they were usually symptom-free on the second or the third day. The major side-effect of resperine therapy was a significant drop in blood pressure, which occurred in 26 of the 163 patients.

Fifty-five patients of the second group were given 5 mg. of perphenazine (1 cc. intramuscularly) on admission. This dose was repeated in 1 hour and again in 3 hours. Most patients received 15 to 20 mg. intramuscularly within 4 to 6 hours. This was followed by oral administration in a dose of 4 mg. every 6 hours. The remaining 59 patients were given a higher dose of perphenazine, namely, 10 mg. administered intramuscularly when treatment was instituted; this dose was repeated after one hour, and thereafter 5 mg. was given as necessary. The drug was particularly well tolerated, and no significant side-effects were observed. Perphenazine therapy appears to be more effective and satisfactory than reserpine or any of the other treatments that have been used by the author, including insulin and dextrose. The ease of administration, as well as the relative ease of nursing care, are valuable features. Although some of the patients remained tremulous after treatment, in general, they tended to improve rather rapidly within 12 to 24 hours, which period could be compared favorably with the experience with insulin and dextrose as well as reserpine.

Reserpine Treatment of Hyperthyroidism: Preliminary Report. A. M. de Andino and F. Ramos-Morales. Bol. Asoc. méd. Puerto Rico **50**:267-276 (Aug.) 1958 (In English) [Santurce].

Seven women and a man, between the ages of 23 and 44 years, with hyperthyroidism were treated with reserpine as a sole therapeutic agent at the endocrine clinic of San Juan City Hospital. Clinical symptoms had appeared during periods ranging from 2 months to 4 years before hospitalization; they were severe in 4 cases and mild in 3. Three of the patients had been given methimazole (Tapazole) over periods of 2 weeks to 7 months, but this drug had been withdrawn on account of intolerance or because of lack of therapeutic results. On hospitalization, all the patients reported loss of weight which varied between 3 and 15 kg. (7 and 33 lb.). There was an increase in the basal metabolic rate and the 24-hour test of radioiodine (I^{131}) intake. Reserpine was administered by mouth in daily doses of 0.4 to 1.0 mg. in 3 or 4 fractional doses over periods ranging from 3 weeks to 2 years. The drug was well tolerated by all the patients but one who complained about constant nasal congestion, which disappeared on diminuation of the dose. In most of the patients the body weight became normal or exceeded the normal figures during the course of treatment. The results were excellent in 5 patients, fair in 2, and poor in 1.

In the 5 patients with excellent results, the symptoms disappeared and the pulse and basal metabolic rate became normal after 2 or 3 months of treatment with reserpine. The 24-hour test of I^{131} intake became normal after 8 to 19 months. The goiter disappeared completely within a period which required from 7 months to 2 years of treatment. One of the patients in this group had a remission of long duration, during which she became pregnant and gave birth to a normal child. This is the first case of pregnancy and delivery at full term during a long remission, brought about by treatment of hyperthyroidism with reserpine, which has been published in the literature. The 2 patients who had a fair response to reserpine therapy were treated for only a short period (20 and 30 days respectively). The patient in whom the response to reserpine was poor had received the drug for a sufficient length of time (185 days), but she had previously failed to respond to Tapazole in daily doses of 40 mg. for 7 months and was considered a therapeutic failure. Hyperthyroidism in this case was eventually controlled by the administration of I^{131} in the therapeutic dose of 4 mc. The satis-

factory results obtained in 7 of these cases seem to justify the use of reserpine in the treatment of hyperthyroidism in a larger number of patients.

Diamidinodiphenylamine Dihydrochloride in the Treatment of a Histoplasmosis Case. V. H. Stapff and J. E. Mockinnon. An. Fac. med. Montevideo 43:116-121 (May-Aug.) 1958 (In Spanish) [Montevideo, Uruguay].

A 46-year-old man was hospitalized at the Hospital de Clinicas of the University of Montevideo, complaining of an illness of 3 months' duration. Besides asthenia and a loss in weight of 12 kg. (26 lb.), he exhibited extensive buccal and oropharyngeal ulcerations which caused acute pain when speaking or eating or during deglutition. He complained of moderate fever and chronic bronchitis with occasional cough. Roentgen-ray examination of the chest showed bilateral infiltration of the lungs (though mainly of the left lung) without cavitation. Histological examination of the sputum revealed tubercle bacilli, and inoculation of this sputum into guinea pigs caused tuberculosis. A biopsy of the oropharyngeal ulcerated region and cultures showed Histoplasma capsulatum; but inoculation of the biopsy material into guinea pigs did not produce tuberculosis. The intradermal reaction with histoplasmin was weakly postive; the tuberculin skin reaction was positive. A diagnosis of oropharyngeal histoplasmosis and of pulmonary tuberculosis associated with pulmonary histoplasmosis was made.

The treatment consisted of intravenous injections of diamidinodiphenylamine dihydrochloride, in daily doses of 150 to 250 mg. in 2 series of 11 and 10 injections, respectively, with an interval of 22 days between the injection series. The total dose of the drug given was 4.6 Gm. The oropharyngeal ulcerations healed and disappeared within 14 days, the satisfactory results obtained becoming more evident after discontinuation of treatment. An 8-month follow-up of the patient showed that there was no recurrence of the oropharyngeal lesions and that there was no further development of either the mild bilateral tuberculosis or the histoplasmosis lesions in the lungs.

PATHOLOGY

A Retrospective Study of Lung Cancer in Women. W. Haenszel, M. B. Shimkin and N. Mantel. J. Nat. Cancer Inst. 21:825-842 (Nov.) 1958 [Washington, D. C.].

Data on smoking habits, complemented by data on age, race, occupation, marital status, and childbearing history, were obtained from 29 institutions which had conducted interviews of 158 women with pulmonary carcinoma. Epidermoid carcinoma was present in 42 patients, adenocarcinoma in 56, and undifferentiated carcinoma in 60. A retrospective investigation revealed that smoking was the largest and only statistically significant item associated with pulmonary carcinoma in this series. The highest risks of epidermoid and undifferentiated types of carcinoma appeared among women using more than one package of cigarettes a day as compared with those who never smoked. The risks were higher for occasional smokers and those who had discontinued smoking than for nonsmokers. The scale of relative risks, according to intensity of cigarette use, was greater for those with epidermoid and undifferentiated carcinomas than for those with adenocarcinomas. No clear correlation between adenocarcinoma and smoking appeared to exist in these patients. Inasmuch as coffee use was included as a control item in this study, only a slight effect, or hardly any, of coffee drinking could be attached to the estimation of relative risks for lung carcinoma. There were no marked risk differences between white-collar workers and non-white-collar workers. No significant effects were found for marital status, pregnancy history, or race. The findings of this study revealed that no sex-linked factor peculiar to lung cancer need be postulated to account for the results on nonsmokers.

Gynecomastia: The Origins of Mammary Swelling in the Male: An Analysis of 406 Patients with Breast Hypertrophy, 525 with Testicular Tumors, and 13 with Adrenal Neoplasms. N. Treves. Cancer 11:1083-1102 (Nov.-Dec.) 1958 [Philadelphia].

Gynecomastia in the male was observed in 406 patients admitted to the breast service, department of surgery, Memorial Center for Cancer and Allied Diseases, New York, during the 23 years between 1932 and 1955. In addition to the data from this service, the histories of patients from the urologic service of Memorial Center were analyzed for the incidence of genecomastia, including 525 patients with testicular tumors and 13 with adrenal neoplasms. Reviewing the cases of the 406 patients, the author says that the constant increase in the number of patients with gynecomastia, observable during each successive 5-year period, reflects not an actual increase but rather an increased cancer consciousness. The number of patients analyzed does not reflect the actual incidence of gynecomastia in that many individuals take no notice of unilateral or bilateral swelling of the breasts.

Gynecomastia occurred predominantly during puberty and adolescence, with a second highest incidence during the "male climacteric" years. The lesion was predominantly unilateral except when produced by testicular or adrenal neoplasms; nodes were enlarged in about one-third of the patients. The location of the mass was usually central (the lesion in male breast cancer is usually excentric).

Nipple abnormality was rare. Trauma was recalled by 14% of the patients; 24% of the patients were found to have, or to have had, endocrine disorders, including general endocrine imbalance and pituitary, thyroid, testicular, and prostatic disorders. Breast cancer did not develop in any of the patients in whom there was a previously recorded or a concomitant diffuse breast hypertrophy. Of the 406 patients, 260 were adequately followed. Of the 136 untreated patients, 115 had complete clinical regression (85%). Among the group that was observed clinically, 6 treated patients and 21 untreated showed no change. Of 124 treated patients (surgery, testosterone therapy, or both), 117 showed satisfactory results (94%). The high figures reflect the fact that the untreated patients were those with mild disease or those who were expected to recover spontaneously without treatment.

The study of patients with testicular tumors revealed a 10% incidence of gynecomastia. There was a similar incidence associated with benign testicular abnormalities. When associated with malignant testicular tumors, gynecomastia was usually bilateral and irreversible (regression did not follow orchiectomy). Of the 13 patients with tumors of the adrenal gland, 11 had tumors of the cortex and 2 of the medulla. Gynecomastia did not occur in the 2 patients with tumors of the adrenal medulla, but 6 of the 11 patients with malignant adrenocortical tumors had bilateral gynecomastia.

While endocrine imbalance is considered the dominant etiological factor of gynecomastia, other conditions that may cause gynecomastia are nutritional deficiencies, administration of estrogen or androgen for therapeutic purposes, liver disease, and testicular, adrenal, or hypophysial tumors. Trauma calls attention to but does not cause gynecomastia. Gynecomastia occurs as a benign lesion that not infrequently will regress spontaneously. Preponderantly of endocrine origin, its importance rests primarily upon the fact that it may be associated with other important and serious concomitant medical problems. Any unexplained gynecomastia, especially bilateral, indicates the necessity for thorough and extensive diagnostic studies.

Effects of Anthihypertensive Treatment on the Evolution of the Renal Lesions in Malignant Nephrosclerosis. L. J. McCormack, J. E. Béland, R. E. Schneckloth and A. C. Corcoran. Am. J. Path. 34:1011-1021 (Nov.-Dec.) 1958 [Ann Arbor, Mich].

Malignant nephrosclerosis is nearly always associated with severe, persistent elevation of resting diastolic arterial pressure and with other symptoms and signs of the syndrome of malignant hypertension. If treatment does not restore arterial pressure to normal levels, the course of the disease is usually marked by rapidly progressing renal failure; this terminates in death of some 80% of patients within one year of the onset and of virtually all by the end of 5 years. It has been demonstrated that remissions of this syndrome can be brought about by a variety of measures—lumbodorsal sympathectomy, treatment with bacterial pyrogens or tissue extracts, and (during the past 6 years) the administration of one of a variety of potent antihypertensive drugs that have in common the capacity to lower diastolic arterial pressure. There have been reports indicating that the treatment of malignant hypertension with potent antihypertensive drugs greatly alters the evolution of renal vascular lesions in this disease.

The authors studied the lesions in sections procured from kidneys of 100 patients who had had malignant nephrosclerosis and on whom autopsies were performed. Nineteen of these had been under treatment with antipressor drugs. Treated patients, especially those who had been under therapy for long periods of time, almost always exhibited remission and healing of the acute arteriolar lesions —thrombosis, thrombonecrosis, and glomerular necrosis. These patients also showed a noteworthy alteration in the nature of the vascular disease. Large and medium-sized renal arteries revealed subintimal fibroplasia with progression to occlusion in some vessels. It is this lesion which presumably leads to the slowly progressive renal failure which was the cause of death in a majority of the treated patients in the group. The observations substantiate the clinical inference that patients with therapeutically induced remission of malignant hypertension exhibit an increased incidence of arteriosclerosis and its complications. This presumably reflects the damage inflicted upon the arteries during the pretreatment period of uncontrolled hypertension. The lesions observed in treated patients correspond to those encountered in hypertensive rats receiving a potent antipressor agent.

A Study of Arsenic in Regular-Sized Unfiltered and Filtered Cigarettes. R. H. Holland, R. H. Wilson, A. R. Acevedo and others. Cancer 11:1115-1118 (Nov-Dec.) 1958 [Philadelphia].

The authors point out that it is now generally agreed that arsenic is carcinogenic to man. In 1947 Neubauer reported 143 medicinal and 24 occupational arsenical cancers. In 1956 Hueper was able to compile 23 cases of carcinoma of the lung, recorded during the preceding 75 years, in which arsenic was considered to be the occupational carcinogen. More recently, Roth found 12 lung cancers in autopsies on 27 vineyard workers who had used arsenical sprays. Lull and Wallach reported a lung cancer mortality rate among males of 145.7, 48.6, and 46.3 per 100,000 population, respectively, in 3 copper-mining-and-smelting counties in Montana. The authors also show that the arsenic content of regular-sized, unfiltered American cigarettes has

increased from 7.5 to 30.0 ppm in 1932-1933 to 42.5 to 52.0 ppm in 1957, an increase of 200 to 600%. Two kinds of Turkish cigarettes and one kind of low-nicotine cigarettes contained 8.2, 6.3, and 10.8 ppm of arsenic, respectively, in 1957. This increase in the arsenic content of cigarette tobaccos in the past 25 years is attributable to the use of arsenic insecticides.

Because of the recent trend toward smoking filtered cigarettes, a study of the effectiveness of filters in removing arsenic from the puffed smoke was carried out. Seven leading brands of filtered cigarettes were tested as to the arsenic content of the cigarette and filter prior to smoking and of the filter, butt, and ash after smoking. The distribution of arsenic in smoking the average, regular-sized, unfiltered cigarette that contains 45 mcg. of arsenic as arsenic trioxide is shown in a diagram. After the cigarette is smoked, 14 mcg. of the arsenic is in the butt, 15 mcg. in the ashes, and 16 mcg., or 35.5% of the total, is volatilized in smoke. It has also been estimated that, when two-thirds of an average-sized, unfiltered cigarette is consumed, 4.95 mcg. of arsenic trioxide will be inhaled. A study of the effectiveness of cigarette filters in removing arsenic from the puffed smoke indicates that only 0.5 to 1.9 mcg. of the arsenic in the puffed smoke is removed by the filter. Although the evidence linking the arsenic in cigarette smoke with lung cancer is highly suggestive, it is felt that a sober approach to the problem with clinical and laboratory studies is needed to prove or disprove the hypothesis.

RADIOLOGY

Intravenous Angiocardiographies: An Analysis of 660 Cases. A. Castellanos, O. Garcia and E. Gonzalez. Acta radiol. **50**:261-272 (Sept.) 1958 (In English) [Stockholm].

Intravenous angiocardiography utilizing a superficial vein of the upper or lower extremity was carried out in 660 patients in Havana, Cuba. Most of the patients were children; 190 were less than 1 year old, and 180 were between the ages of 1 and 2 years. The number of patients decreased sharply in the age group between 11 and 12 years; only 30 patients between the ages of 20 and 30 years underwent intravenous angiocardiography, and none of the patients subjected to this examination was older than 40 years. The volume of the contrast medium injected varied most frequently between 1.1 and 1.5 cc. per kilogram of body weight. Larger doses were administered in selected patients after due consideration of the topography of the vessel through which the injection was to be made, the concentration of the contrast medium, the size of the heart, and the clinical state of the patient. The left basilic vein was used most frequently. This is explained by the fact that cardiac catheterization preceded the angiocardiography. The 2 jugular veins were used in 180 children; the jugular vein is the vessel of choice in infants, aged less than one year, because of the short distance between the site of the injection and the right cardiac chambers. The injection time was recorded in 538 patients, and in 463 of these the injection was made in one second or less, i.e., within the time generally considered best for obtaining the most satisfactory results. A concentration of 70% contrast medium was used in 647 (98%) of the 660 patients. Sodium acetrizoate (Urokon) was employed in 339 patients and iodopyracet (Diodrast) concentrated in 312 patients. A Castellanos no. 10 cannula was used in 6.3% of the patients and a Castellanos no. 12 in 33%.

There were 44 slight, medium, and serious side-reactions, most of which were the result of toxicity of, and hypersensitivity to, the chemicals employed as contrast mediums. Allergic effects characterized by coryza and urticarial rash were observed in 4 patients. Death resulted from angiocardiography in 6 patients, representing a mortality rate of less than 1%. Three of these 6 patients had an extreme degree of tetralogy of Fallot, 1 had a three-chambered heart, 1 had fibroelastosis, and 1 had total transposition of the great vessels with auricular fibrillation. Five of these 6 patients were less than 16 months old, and the one patient with marked auricular fibrillation was 17 years old. Every one of the infants who died was cyanotic. Four rules must be followed in the performance of intravenous angiocardiography: 1. The injection should be made into the veins nearest the heart. 2. The highest possible concentration and the smallest volume of contrast medium should be used. 3. The contrast medium should be injected as rapidly as possible. 4. The largest cannula consistent with the vein chosen for the injection should be employed. Intravenous angiocardiography, as opposed to cardiac catheterization, remains the method of choice for providing correct and complete diagnostic information in pediatric cardiology.

Results of Roentgen Treatment of Acromegaly: A Clinical Review. B. Arner, M. Lindgren and B. Lindqvist. Acta endocrinol. **29**:575-586 (Dec.) 1958 (In English) [Copenhagen].

The course of acromegaly is unpredictable, for which reason caution must be exercised in the evaluation of the effect of treatment. For many years symptoms of compression of the optic nerve have been, and still are, an indication for operation. However, most neurosurgeons regard patients with acromegaly as poor operative risks because of the danger of hemorrhage in the operative field. It is

possible that the modified transnasal approach, described in 1956, might reduce the risks attending hypophysectomy. It is also possible that ultrahard radiation and the stereotactic technique will make it possible to deliver hitherto unattainable doses to the hypophysis. There is reason to expect that more radical methods will control those symptoms of acromegaly due to hormonal hyperfunction of the hypophysis, but these results can only be achieved at the price of panhypopituitarism. Advances made during the last decade in endocrinology have now provided good substitution therapy.

It was against this background that the authors reviewed in 1954-1955 the records of 20 patients with acromegaly treated during the period from 1922 to 1953 by roentgen-ray irradiation only. Nineteen patients had no symptom of compression of the optic nerves; one patient had a large visual-field defect which was considerably diminished by roentgen-ray treatment. This therapy was accompanied by a certain regression of swelling of the soft tissues in the parts of the body involved; no regression was observed in the acromegalic growth disorders of the skeleton. In none of the cases was it necessary to operate because of optic nerve complications during the later course of the disease. The late prognosis as to life was good in the present material, and there was no excessive morbidity from cardiovascular disease.

BIOCHEMISTRY

The Serum Trihydroxy-Dihydroxy Bile Acid Ratio in Liver and Biliary Tract Disease. J. B. Carey Jr. J. Clin. Invest. **37**:1494-1503 (Nov.) 1958 [New York].

Serum bile acid determinations (chiefly cholic acid) have been of little value in the study of hepatobiliary disorders. There has been no agreement concerning either the quantity or the nature of the bile acids alleged to be present in normal serum. More recently studies showed that bile acids are demonstrable by paper chromatography in most normal human serums and that these acids are the same as those in bile and occur in approximately the same relative proportions. The author describes a quantitative method for the simultaneous differential determination of serum trihydroxy and dihydroxy bile acids. Normal values were established for healthy subjects. The author found that the serum concentrations of either the trihydroxy or the dihydroxy bile acids were commonly elevated in patients with hepatobiliary disease, and although this information was not especially helpful, it became apparent that the ratio of the 2 main bile acid types often separated the patients into 2 groups. Those with predominantly hepatocellular injury had a trihydroxy-dihydroxy ratio of less than 1. whereas those with obstructive jaundice usually had a ratio of greater than 1. The dihydroxy acids predominated in the serum of patients with Laennec's cirrhosis, whereas patients with obstructive jaundice tended to have higher concentrations of trihydroxy acids.

Bile acid determinations were made on serums of 41 patients in whom the diagnosis of biliary obstruction or parenchymal liver disease was confirmed by laparotomy, biopsy, peritoneoscopy, or autopsy, and all of these are included in this report. It was found that with severe liver injury a disproportionate increase in the dihydroxy bile acid concentration reduced the trihydroxy-dihydroxy ratio to less than 1. Persistence of this reversed ratio is frequently followed by coma, death, or both. When the ratio is only temporarily reversed, as with acute or transient liver injury, improvement or recovery of the patient is paralleled by a rise in the ratio toward a value of 1 or more. This is helpful in estimating the extent of liver injury and monitoring its course. With biliary obstruction, whether intrahepatic or extrahepatic, the serum bile acid concentrations are increased, but the ratio remains greater than 1.

The Oxytalan Fiber: A Previously Undescribed Connective Tissue Fiber. H. M. Fullmer and R. D. Lillie. J. Histochem. **6**:425-430 (Nov.) 1958 [Baltimore].

Analysis of complete autopsies performed on rats, mice, and guinea pigs and analysis of selected human tissues obtained from autopsy and surgical specimens revealed a separate connective tissue fiber, distinct from the collagenous, elastic, and reticular varieties, for which the authors coined the term "oxytalan fiber." Oxytalan fibers were found only in the periodontal membranes, tendons, ligaments, adventitia of blood vessels, connective tissue sheaths surrounding skin appendages, and epineurium and perineurium. They were not found in other connective tissues, such as normal and aging dermis generally, granulation tissue, and parenchymatous organ stroma. Their distribution appeared to be restricted to sites where connective tissues are subjected to stress.

Staining tests showed that, after peracetic acid oxidation, the oxytalan fibers stain with aldehyde fuchsin, orcein, and resorcin fuchsin; they fail to react with orcinol-new fuchsin and Verhoeff's stain for elastic tissue. The stainable material in oxytalan fibers is slowly removed by lysozyme, and by testicular hyaluronidase after peracetic acid oxidation, and is believed to be a mucopolysaccharide. There is no observable effect on elastic fibers similarly treated. Elastase does not digest Formalin-fixed oxytalan fibers except after peracetic acid oxidation. A protease contaminant in elastase was noted.

BOOK REVIEWS

Injuries and Surgical Diseases of the Ischium. By Henry Milch, M.D., Attending Orthopedic Surgeon, Hospital for Joint Diseases, New York. Cloth. $10.50. Pp. 163, with 106 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1958.

This monograph covers all phases of disabilities of the ischium, but is difficult to read and requires great concentration. The anatomy of the ischium and its evolutionary development makes interesting reading. The line drawings, however, particularly those of muscle origin and insertion, are difficult to follow. For the orientation of the reader it would have been much better had this been shown in color. The roentgenographic reproductions throughout the book are not good; mostly they are too dark, and it has been necessary for the author to use arrows to point out what is being described in the text. As a reference book on all disabilities of the ischium this is a worthwhile work but not a ready reference book for the medical student or house staff. It is appreciated that the author has brought into one volume all of the facts about the ischium, and he should be commended for the effort and interest that he has taken in writing the book.

System of Ophthalmology. Edited by Sir Stewart Duke-Elder, G.C.F.O., M.A., LL.D. [To be in 15 volumes.] Volume I: The Eye in Evolution. By Sir Stewart Duke-Elder. Cloth. $27.50. Pp. 843, with 1,267 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3; Henry Kimpton (medical book department of Hirschfeld Brothers, Ltd.), 134 Great Portland St., London, W. 1, England, 1958.

This is a wondrous, factual, epic story of the development and evolution of the eye from the effect of light on the undifferentiated protoplasm of the ameba to the highly efficient visual sense of the birds. The importance of pigment as an essential feature of photoreceptors is interestingly presented. The description of the different functional characteristics of the visual apparatus of all phyla of the animal kingdom is fascinating. The necessary and multitudinous expedients adopted by an organ of sight to meet the requirements of environments as completely different as the darkness of the ocean and the pure light of the upper air, and habits so diverse as the quasi-immobility of a parasite and the constant activity of a bird of prey, are beautifully related. The author constantly compares the attributes and inefficiencies of one species of animal with those of another. The exigencies of nocturnal and diurnal vision are met by variations in the size, shape, and motility of the pupil and by the provision of a tapetum, choroidal or retinal, augmenting the amount of light by its mirror-like effect. Visual acuity is provided by the area centralis or fovea; stereopsis through a swing forward of the visual axes, the location, shape, and movement of the lens proper in certain fishes, and the development of accessory retinas in certain fishes.

The unusual variation in color of the irises of birds meets the specific needs and functions of each species. The development of the proficient sight of the owl, which, even though its eye is especially adapted for nocturnal vision, will detect a hawk approaching in the daylight sky at a height at which it is invisible to man even though its wing spread might be 15 ft., is truly remarkable. The chapter on bioluminescence is one of the most captivating in the book. The author presents interesting information about and spectacular photographs of luminous and electric organs of fish. This is the first time that this subject matter, which forms the very basis of the development and science of sight, has been gathered together in a single book. The numerous marginal sketches are a welcome addition. The zoological glossary is a novel feature. Any student of science, biology, or ophthalmology who has had the privilege of reading any of the author's works before should be looking forward to the other volumes of this series.

Applied Medical Library Practice. By Thomas E. Keys, A.B., M.A., Librarian, Mayo Clinic, Rochester, Minn. With chapters by Catherine Kennedy, B.S., L.S., Associate Librarian, Mayo Clinic, and Ruth M. Tews, B.S., L.S., Hospital Librarian, Mayo Clinic. Cloth. $10.75. Pp. 495, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

In this welcome addition to the files of library literature, the author states that the book is designed to teach the physician how to use a medical library for research. To this end he describes what is in a library, how it is arranged, how to use the indexes and guides to its contents, and how to locate the desired materials. This coverage includes such fields as the administration of the library and the cataloging of its contents. A useful chapter on medical indexes describes, compares, and evaluates the various indexes and tells how to use them to compile a bibliography. A later chapter teaches how the bibliography itself should be prepared. There is a good discussion of abstract journals and how to use them and a chapter on how to collect and arrange a reprint collection. Research libraries and private medical libraries are described. One

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

chapter lists 78 representative medical libraries in the United States, describing the purpose, scope, size, and loan policies of each. This is useful for physicians who have no library facilities at hand. Some valuable and interesting facts on the history of medical books and medical publishing provide useful reference data. A final chapter on changing concepts in library service gives the reader a look into the future. There are valuable lists of publishers and dealers in the appendix. The style is extremely readable. References follow each chapter. The print is good, and the index is comprehensive. This volume furnishes, for the physician using a medical library, the same type of information and assistance that the Medical Library Association's handbook of medical library practice offers for the librarian, but the information itself is not the same. It has a definite place on the bookshelf of any doctor, student, or librarian who has occasion to use the research facilities of a medical library.

The Extra Pharmacopoeia, Martindale, Incorporating Squire's Companion. Volume I. Published by direction of Council of Pharmaceutical Society of Great Britain. Twenty-fourth edition. Cloth. 65 shillings. Pharmaceutical Press, 17 Bloomsbury Sq., London, W. C. 1, England; [Rittenhouse Book Store, 1706 Rittenhouse Sq., Philadelphia 3] 1958.

The Extra Pharmacopoeia, originally produced by William Martindale in 1883 and now published by the Pharmaceutical Society of Great Britain, contains information on the drugs presently used in Great Britain. This edition has been entirely revised, reset, and increased in size because of the addition both of new drugs and of new material on drugs already described in previous editions. Although this edition appears only six years after the 23rd edition, it was necessary to increase the size by almost 350 pages. The general section contains about 1,400 pages of drug descriptions listed in alphabetical order under English titles. It was found to be convenient, however, to group certain classes of drugs such as the sulfonamides, the barbiturates, and a few others. Included under the specific drugs are a dosage statement, a brief physical description of the compound including solubilities, toxic effects, and incompatibilities, antidotes, contraindications, uses, sizes available, and proprietary preparations containing the drug. Many of these monographs contain brief abstracts of pertinent literature and references to original articles. Also included in this section are supplementary lists of drugs, with proprietary preparations containing them, that are of interest but are not as widely used as those in the general list.

The book also contains special sections on antibiotics, immunological agents, and radioactive isotopes. The antibiotic section, in addition to including the usual material on drugs, contains a discussion of the use of antibiotics in specific diseases and a chart on antibiotics selection. The volume includes a useful therapeutic and general index. Although the book lists drugs used chiefly in Great Britain, and is based mainly on the British Pharmacopoeia and the British Pharmaceutical Codex, pharmacopoeias of many other countries were also consulted and used. The book deserves wide use in the United States.

An Atlas of Esophageal Motility in Health and Disease. By Charles F. Code, M.D., Ph.D., Professor of Physiology, Mayo Foundation, Rochester, Minn., and others. Cloth. $8.50. Pp. 134, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

This atlas is a record of motility studies of the normal and diseased esophagus. The technique of obtaining esophageal pressures at various levels is described and the instruments used are excellently illustrated. Tracings obtained at various levels during resting phases and deglutition are shown, with brief explanations directly under the tracings or on the facing page. Various representative curves are enlarged and the significant information they reveal is described and explained. The remainder of the book is clear and concise, including tracings of intraesophageal pressures in such conditions as achalasia, diffuse esophageal spasm, and scleroderma. Interesting phenomena of response to stimuli obtained from medication are also illustrated. This book should be of interest to clinicians and physiologists who deal with the problems of the gastrointestinal tract. It is admittedly limited in scope, although from the title one would expect a more comprehensive analysis of esophageal motility. The motility in such conditions as caustic strictures, neoplasms, and diverticula is not shown.

Patients, Physicians and Illness: Sourcebook in Behavioral Science and Medicine. Edited by E. Gartly Jaco, Associate Professor of Medical Sociology, University of Texas Medical Branch, Galveston. Cloth. $7.50. Pp. 600. Free Press, Glencoe, Ill., 1958.

This volume is put forth as a source book, an effort to present in compact fashion the ideas of various representatives of the behavioral sciences on different aspects of the art and science of medicine. It attempts to bridge the gap between two disciplines which, though still widely separated, have taken some steps toward *rapprochement*. These steps have been made necessary by the changes in the concepts of disease and in the practice of medicine. Recognition of the place of the behavioral sciences in medicine has been slow to come about; but gradually behavioral scientists are being introduced into medical school faculties and hospital staffs, and attention is being given to courses in human behavior and to the impact of cultural and social factors beyond the scope of the biological sciences on human life.

The 55 short chapters in this book are written by 63 contributors. Many of the chapters should be of interest to the physician and all of them to the medical educator and administrator, for they mark significantly the changing practice which seems to be in the offing as the population increases and as functional and geriatric ills occupy more of our attention. Also, the change in the locus of medical practice from the home to the physician's office and the hospital has led to changes in that essential factor in all treatment, the physician-patient relationship. With the rise of specialization, the patient loses that close relationship he once had with the family physician and becomes fragmented and divided among various specialists. The more fragmented he becomes, the more fragmentary is his relationship with the physician, and this change is becoming more marked each year. Though we may not like some of these changes it is wise for us to know about them, and this book serves a useful function by showing how modern medical practice looks to trained objective observers.

Regional Ileitis. By Burrill B. Crohn, M.D., and Harry Yarnis, M.D. With special contributions by Richard H. Marshak, M.D., and David A. Turner, Ph.D. Second edition. Cloth. $7.25. Pp. 239, with 81 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W. C. 1, England, 1958.

The author of this monograph is the originator of the concept of regional ileitis as a disease entity. The book covers both regional ileitis and a group of allied granulomatous diseases occurring in other portions of the intestine. The literature to date is surveyed and the author also presents his own extensive experience in treating over 500 patients with ileitis and an additional 100 with inflammatory disease in other segments. There are valuable data on the natural history of the disease and the expectation of treatment by medical and surgical means. Radiographic diagnosis and malabsorption are covered in separate chapters by additional authors. In spite of feeble editing, the book is a valuable reference work for gastroenterologists, surgeons, radiologists, and others who have an interest in this puzzling disease.

Young Endeavour: Contributions to Science by Medical Students of the Past Four Centuries. By William Carleton Gibson, D.Phil., M.D., C.M., Kinsmen Professor of Neurological Research, University of British Columbia, Vancouver. With foreword by Sir Henry Dale, O.M. Cloth. $6.50. Pp. 292, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

"We must," says the author of this book, "encourage enquiring minds in medicine." In 12 chapters filled with lively details he tells the stories of the many men in the history of medicine who either made outstanding discoveries in their student days or clearly laid the foundations when they were young for later discoveries. In the last chapter he discusses the old questions of how to prevent the academic atmosphere from becoming stagnant with orthodoxy and conformity, how to create conditions favorable to discovery, what it is that produces a scientific bent in some people even in childhood, and how one man could accomplish what he did while "living on radishes and bread and the charity of a hospital for incurables in Italy" while another subsisted on "eggs and milk and the charity of a pioneer hospital in Ohio." Committees on admission to modern medical schools should find food for thought in the account of one young scapegrace whose mother, named Temperance, sent him off to college "with a Dutch liquor case containing six large bottles filled with various kinds of strong waters . . . enough to craze a whole class of young bacchanalians." Was this a help or a hindrance to his subsequent magnificent career? This book deserves to be widely read, for it should fascinate and inspire anyone who picks it up.

Pediatric Methods and Standards. Editor: Fred H. Harvie, M.D., Associate Professor of Clinical Pediatrics, Department of Pediatrics, School of Medicine, University of Pennsylvania, Philadelphia. Third edition. Paper. $4.50. Pp. 324, with illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1958.

This small compendium can be easily carried in a physician's bag or in his pocket. It can be used as a quick source of information in pediatrics for the general practitioner. As the author rightfully states, the text is not intended to be all-inclusive nor to contain controversial subjects. For such a small volume it contains a tremendous amount of information. Laboratory procedures are described and this makes a unseful addition to the book.

Poisoning: A Guide to Clinical Diagnosis and Treatment. By W. F. von Oettingen, M.D., Ph.D. Second edition. Cloth. $12.50. Pp. 627. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1958.

This second edition of a well-known book deals with the practical aspects of the diagnosis and treatment of poisoning. The author has retained the original format but added a valuable discussion of the potentially dangerous side-effects of therapeutic agents. The material is organized under four main sections. Part 1 contains chapters on the classification and diagnosis of poisoning, medicolegal responsibilities, emergency measures, and equipment. Part 2 describes pathological changes of organs and their functions that may be observed in a medical examination. Signs and symptoms, classified by body systems, are followed by an enumeration of chemicals and drugs which have been reported to cause such effects, biochemical and biophysical changes in the blood and urine and agents which might cause them, and laboratory tests for the

detection of toxic substances in the blood and urine. Part 3 is concerned with the rationale of treatment, techniques for aiding the removal or elimination of the toxic agent, detoxification, symptomatic treatment, and general measures for the treatment of aftereffects. Part 4 provides short descriptions of 575 poisons arranged alphabetically. A synopsis of clinical findings and instructions for treatment are given under each poison along with references for more detailed study. This book is highly recommended for the practitioner and should be available as a standard reference at poison-control centers.

Cardiovascular Sound in Health and Disease. By Victor A. McKusick, M.D., Associate Professor of Medicine, Johns Hopkins University School of Medicine, Baltimore. Comprehensive treatise, introduced by historical survey, illustrated mainly by sound spectrograms (spectral phonocardiograms) and supplemented by extensive bibliography, with section on respiratory sound. Cloth. $15. Pp. 570, with 494 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2, 1958.

The author of this monumental work has gone into great detail in describing how the cardiac sounds and murmurs are produced and how they can best be recorded. There is an excellent chapter on the stethoscope and the art and practice of cardiac auscultation. Phonocardiography is fully described, taking into account the advantages and limitations of various methods used. The recording method used by the author is known as spectral phonocardiography, an application of the method of sound spectrography developed at the Bell Telephone Laboratories. The sound recording is usually first made on magnetic tape. Then a segment of sound is selected for analysis and played over on the edge of a magnetic disk. This permits repeated playback. Visual records of the sound can be made at different frequency bands for analysis. Records of heart sounds and murmurs have become increasingly important in recent years as part of the determination of a patient's suitability for cardiac operations and also in evaluating the results of such operations. Variations in heart sounds and murmurs in a number of cardiac conditions are fully described, accompanied by many illustrations, mostly from the author's files. This excellent source book should be especially valuable for the cardiologist and should be useful also to the general internist.

Modern Trends in Anesthesia. Edited by Frankis T. Evans, M.B., B.S., F.F.A.R.C.S., and T. Cecil Gray, M.D., F.F.A.R.C.S. Cloth. $15. Pp. 318; 13, with 30 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16; Butterworth & Co. (Canada), Ltd., 1367 Danforth Ave., Toronto 6, Canada, 1958.

This publication is unlike most textbooks on anesthesiology. It should be classified not as a textbook but rather as a series of monographs, contributed by 22 authors one of whom is the senior editor of the book. This is definitely not a book from which to teach the fundamentals of anesthesia or techniques for its application; it is rather a collection of scholarly essays on the most important phases or trends in anesthesia as presently practiced. The authors did not select anesthetists exclusively as contributors. They have, for example, enlisted the aid of a psychiatrist to present an essay on hypnosis, a surgeon on cardiorespiratory pumps, and a pharmacologist and a physiologist for other appropriate chapters. Except in the chapter on pumps there are few illustrations. These essays cover such subjects as drugs, pulmonary and circulatory physiology, hypothermia, anoxia, fatalities, and research. Since the authors are mostly from England there are occasional statements that are not applicable in the United States, for instance, that cyclopropane is not being used as often as formerly in England. In the United States its use has increased steadily since the war. This book is a delight to read and should be appreciated by specialists in this field, and particularly by teachers. It is written not for the medical student or the beginner but for the specialist by specialists. It is well printed with easily readable type. References are found at the end of each chapter and there is a good index.

A Text-book of X-Ray Diagnosis. Volume III. By British authors. In four volumes. Edited by S. Cochrane Shanks, C.B.E., M.D., F.R.C.P., Director, X-Ray Diagnostic Department, University College Hospital, London, and Peter Kerley, C.V.O., C.B.E., M.D., Director, X-Ray Department, Westminster Hospital, London. Third edition. Cloth. $23. Pp. 883, with 802 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1958.

In this new edition the subject matter has been revised in keeping with advances made in diagnostic roentgenology since the last edition in 1950. A total of 53 pages and 108 illustrations have been added to the new volume. It is divided into six parts: the alimentary tract; the biliary tract; the liver, spleen, and adrenals; radiology in obstetrics; gynecologic radiology; and the urinary tract. Each section is well illustrated, with the reproductions in the positive phase. The subject matter is presented in a concise manner that is easy to read and includes much useful data on incidence, etiology, pathology, clinical features, and, where indicated, technical aspects. This highly respected text has long since become a classic for English-speaking physicians, representing one of the most comprehensive and informative works covering the entire area of roentgenographic diagnosis. This third edition should earn the same success enjoyed by the previous printings. It is highly recommended not only to the graduate student in radiology but to his preceptor as an essential addition to his library. Any physician interested in diseases within the abdomen should find this work a storehouse of information.

QUESTIONS AND ANSWERS

MUCOVISCIDOSIS

To the Editor:—*Three siblings, aged 7 months, 8 years, and 13 years, have the disease known as mucoviscidosis. Is there any new therapy for this condition? What is the value of such preparations as streptokinase-streptodornase and trypsin? Would mucolytic aerosol therapy, with or without antibiotics, be of any help? The children already receive multiple vitamins, vitamin C in addition, and pancreatic extracts.*

George C. Mosch, M.D., Coudersport, Pa.

Answer.—Three siblings in one family affected with mucoviscidosis suggests that both parents are homologous carriers of the recessive character and that the probability of other siblings being so affected is great. Streptokinase-streptodornase and trypsin have been used, with inconsistent results reported. Mucolytic aerosol therapy, with or without antibiotics, has had some success. Since this disease represents a defect in metabolism, the severity and systems involved may be quite varied. The main basic concept is maintenance of nutrition and avoidance of respiratory infection. The ease with which this is accomplished is determined somewhat by early recognition of the disease. If the respiratory tract involvement can be minimized, the outlook can be improved. Aqueous (water soluble) solutions of vitamins are more readily absorbed than other forms.

To the Editor:—*Six years ago a woman lost an only child, a daughter about 3 years of age. The cause of death (no autopsy was performed) was said to be cystic fibrosis of lungs and pancreas. Since that time she had no more children because, as she has been told frequently, the chances are that any further children would also be so afflicted. Is this true? If so, what are the odds that she will have a normal child?*

Willard J. Lloyd, M.D., New Hartford, N. Y.

Answer.—Fibrocystic disease of the pancreas with accompanying fibrosis of the lungs is inherited. Most studies indicate it is a Mendelian recessive character. Many investigators suggest that about one child in four will be affected. This consultant would be inclined to urge the patient to have another child as soon as possible. Early detection and treatment could have an effect on the progress of the disease if the next child should be affected.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

MENOPAUSE AND CONCEPTION

To the Editor:—*Patients in the menopause often ask how long after cessation of the menstrual period conception is possible. Please give an opinion, with reference to women 47 to 52 years of age and not to those who stop menstruating at the end of the fourth decade. The literature contains contradictory reports on this subject. Are examinations of smears of the vaginal epithelium of any value?*

Ludwig Gruenewald, M.D., Sheboygan, Wis.

Answer.—Pregnancy in women over 47 years of age is rare, even in those who continue to menstruate beyond this age. In 65,000 deliveries at the Johns Hopkins Hospital, there was only one such case; this occurred in a feeble-minded nonwhite woman who stated she was 49 but may not have known her correct age (Eastman, Williams Obstetrics, ed. 11, New York, Appleton-Century-Crofts, Inc., 1956, p. 218). At the Boston Lying-in Hospital, the oldest known patient to be delivered was 49 (Newell and Rock, *Am. J. Obst. Gynec.* **63**:875, 1952). At the Chicago Lying-in Hospital, in over 50,000 deliveries there were two women of 46 and two of 48 years of age who gave birth (Davis and Seski, *Surg. Gynec. & Obst.* **87**:145, 1948). DeLee and Greenhill each delivered a woman 52 years of age (Greenhill, Obstetrics, ed. 11, Philadelphia, W. B. Saunders Company, 1955, p. 102). In the review by Newell and Rock of the literature concerning the upper age limit of parturition, it was concluded, "From what we have been able to gather from vital statistics and from medical literature, it appears that parturition in a woman over 52 years of age has not been proved and that, therefore, were it surely to occur in a woman, say of 55, it must be considered a gross aberration of reproduction physiology." Waldeyer (*Zentralbl. f. Gynäk.* **58**:2882, 1934) reported seven proved cases of reactivation of senile ovaries in women. In these patients, follicles developed in the ovaries to the stage of early corpus luteum formation but not to the stage of full bloom. The endometrium developed only to the interval stage. Hence, even though there was reactivation of ovarian function, pregnancy most likely could not have taken place. In view of the foregoing data, women who stop menstruating after 47 years of age, and certainly those beyond 49, may be told that the chances of a pregnancy are too remote for concern. Vaginal smears will not help to determine the possibility of pregnancy in women past the menopause.

*Classification of Patients with Diseases of the Heart**

Functional Capacity		Therapeutic Classification	
Class 1	Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.	Class A	Patients with cardiac disease whose ordinary physical activity need not be restricted.
Class 2	Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.	Class B	Patients with cardiac disease whose ordinary physical activity need not be restricted, but who should be advised against severe or competitive physical efforts.
Class 3	Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.	Class C	Patients with cardiac disease whose ordinary physical activity should be moderately restricted, and whose more strenuous efforts should be discontinued.
Class 4	Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency or of the anginal syndrome are present even at rest. If any physical activity is undertaken, discomfort is increased.	Class D	Patients with cardiac disease whose ordinary physical activity should be markedly restricted.
		Class E	Patients with cardiac disease who should be at complete rest, confined to bed or chair.

No Heart Disease: Predisposing Etiological Factor†
These are patients in whom no cardiac disease is discovered but whose course should be followed by periodic examinations because of the presence or history of an etiological factor that might cause heart disease. It is essential that the etiological diagnosis also be stated.

Undiagnosed Manifestation†
These are patients with symptoms or signs referable to the heart but in whom a diagnosis of cardiac disease is uncertain. Reexamination after a suitable interval will usually help to establish a definite diagnosis. When there is a reasonable probability that the signs or symptoms are not of cardiac origin, this title should not be used and the diagnosis then should be "no heart disease."

* Classification of the American Heart Association, 1953 revision.
† For some patients both diagnoses will apply.

CLASSIFICATION OF HEART DISEASE

To the Editor:—*Please give the criteria set up by the American Heart Association for the evaluation of heart disease and work tolerance. Since the social security forms at this time are asking for this grade and classification, it is not fair to the patient to leave that portion of the form blank and possibly jeopardize his obtaining social security.*

William B. Roudybush, M.D., Muscatine, Iowa.

Answer.—The classification of patients with heart disease, as distributed by the American Heart Association, is shown in the box. Physicians may obtain additional publications and teaching aids from A. H. A. affiliates in their states.

DEPTH PERCEPTION

To the Editor:—*Does depth perception depend on binocular vision? If so, how is it possible for one who has lost all sight in one eye to pass satisfactorily the usually prescribed technical tests used in estimating depth perception? Please give an opinion on the safety of approving the employment of a man with one eye as a crane operator; this person has 20/20 vision in the remaining eye and normal depth perception.*

M.D., California.

Answer.—Depth perception, unlike stereopsis, does not depend on binocularity. Depth perception in a normal person is based on stereopsis plus such monocular depth clues as size (visual angle and experience of known size), brightness, parallax, overlay, perspective, atmospheric haze, and color. The absence of one clue, stereopsis, is not a serious handicap in most occupations. At least one man with only one eye became a champion ski jumper. A crane operator, whose experience has been gained while using two eyes, will require three months or more of experience when one eye becomes blind before he is quite safe in the operation of a crane again. He will gain depth perception mainly by using parallax, in which he moves his head sidewise. Thus a one-eyed man could safely operate a crane, given sufficient experience. Knowing that the public would likely blame any accident on his blind eye, he would be wise to give the utmost care and attention to his task.

DRUGS AND ADRENAL GLAND STIMULATION

To the Editor:—*Do colchicine and salicylates produce sufficient stimulation of the adrenal gland as to be contraindicated in patients with hypertension or tendency to hypertension?*

L. Stolfa, M.D., San Francisco.

Answer.—Various investigations have been carried out in regard to the controversy as to whether in humans a temporary hypofunction of the pituitary adrenal system plays a role in the onset of acute gouty arthritis and as to whether the effect of colchicine is obtained through this pituitary adrenal system. A review of the recent literature (Robinson and others, *Ann. Int. Med.* 45:831, 1956) provides no convincing evidence that colchicine in therapeutic doses in humans acts through the pituitary adrenal system, and the mechanism of its action still remains a mystery. Some evidence is available that a mild retention of sodium and chloride occurs after colchicine administration, but less than after ACTH therapy. Likewise, evidence is lacking in man that salicylates exert their therapeutic action through stimulation of the pituitary adrenal system.

HYPOTHYROIDISM AND CHRONIC LYMPHOMATOUS THYROIDITIS

To the Editor:—*What effect does hypothyroidism have on chronic lymphomatous thyroiditis (struma lymphomatosa, Hashimoto's disease) and on symptoms suggestive of hypoparathyroidism? A patient with 75% of her thyroid removed has a basal metabolic rate of —27%.*

W. J. Tucker, M.D., Ashland, Wis.

Answer.—Hypothyroidism is not known definitely to affect the basic disease mechanism or course of chronic lymphomatous thyroiditis. Theoretically, however, the increase in pituitary thyrotropin, which results as the thyroid hormone output decreases, may accelerate the progress of the disease and result in an increase in the size of the gland. This is suggested by the dramatic decrease in size which may follow replacement therapy with thyroid, presumably due to suppression of the thyrotropin output. Minor surgical interference with the gland in a patient with chronic thyroiditis may precipitate the early onset of hypothyroidism with its typical symptoms. Hypothyroidism and hypoparathyroidism may coexist, with typical symptoms of each. There is usually minimal, if any, modification of the symptoms due to the hypoparathyroidism, and both disorders should be recognized and treated by proper replacement therapy.

SCIATICA

To the Editor:—*A patient has had sciatica for five weeks, and no therapeutic agent has given any appreciable benefit, including five or six ampuls of animal gastric mucosa enzyme given parenterally and corticosteroids. The patient is now taking sodium salicylate, and this gives some relief. At night the pain is worse; in fact, during the day the patient has little pain and is active in his work. Aspirin and pentobarbital are taken and a hot pad used for relief at night. If pain occurs in the daytime, infrared rays and an ointment with methyl salicylate are used. Several months ago, the patient fell and struck his occiput. He was unconscious for a few moments and probably sustained a slight concussion. Could this fall have any connection with the present ailment?*

R. C. Ferguson, M.D., Eastland, Texas.

Answer.—Before attempting to prescribe for relief of what is apparently a severe pain, one would have to have information concerning the motor, reflex, and sensory status of the extremity involved. If any abnormalities are found in the basic neurological tests, x-rays of the lumbosacral area and a spinal fluid examination are indicated. If these findings show any deviation from the normal, an oil myelogram should be made. The term "sciatica" is too vague to warrant symptomatic therapy. One must exclude a sciatic neuritis, discogenic sciatic neuralgia, and metastatic neoplasm, to mention a few possibilities.

IDIOPATHIC SEIZURE

To the Editor:—*A normal appearing, slightly overnourished man, aged 30, had without warning or apparent cause a sudden loss of consciousness with falling. This was followed immediately by a convulsive seizure lasting a few minutes, during which time he bit his tongue. There was no incontinence. After one hour of bed rest, he slowly regained consciousness; he was described as being mentally lethargic and dull. The seizure occurred just prior to the lunch period. Findings on physical examination and personal and family history were entirely negative. Blood chemistry and electroencephalographic examinations have not been done. Hypoglycemia was suggested as probably being causative, since the seizure occurred as the man was walking to his noon lunch. He stated that he had felt well all morning but was hungry because he had omitted his customary candy bar and "pop" at the forenoon coffee break; furthermore, he was emotionally upset. Could this episode be reasonably explained on the basis of hypoglycemia?*

M.D., California.

Answer.—Sudden convulsions occurring in otherwise normal persons, such as this patient, are common. There are 1,500,000 epileptics in the United States, and undoubtedly there are many others who have seizures due to various causes. It is doubtful that hypoglycemia is a factor in true epilepsy. This group has an amazingly stable carbohydrate metabolism. It is difficult to produce an altered curve either on glucose or on insulin tolerance tests. In an experiment by Pollock and Boshes (*Arch. Int. Med.* **59**:1000, 1937), the blood sugar levels of known epileptics who had not had any medication for weeks was lowered almost to 0 and many of them were in the range of 20 mg.%. Not 1 of 97 patients had a convulsion. It is much more likely that this man had an epileptic seizure due to some disturbance in the central nervous system. If this was his first seizure, at the age of 30, one should seek an organic cause, such as brain tumor, residuals of previous brain trauma, infection (encephalitis of viral origin or central nervous system syphilis), alterations of cerebral blood flow associated with various degrees of cortical atrophy, and chronic alcoholism. The examination should include careful physical and neurological examinations, electroencephalographic review, roentgenogram of the skull, spinal fluid studies, air studies and angiography of the brain, and blood chemistry, including blood urea nitrogen and serologic tests. It may be necessary to take more than one electroencephalogram, because the patient may be examined in an

interseizure state when the initial tracing may be normal. The following exceptions to such a survey are worthy of note: People who have diabetes mellitus, an islet tumor of the pancreas, or serious hepatic dysfunction from hepatitis or multiple metastases to the liver may show poor carbohydrate metabolism. This type of patient could conceivably have an epileptic seizure associated with a lowered blood sugar level, but, in the case under question, the patient's history was negative.

KIDNEY STONES

To the Editor:—*The impression has been held that in patients suffering from acute or chronic renal lithiasis the chemical composition of the stone can be determined accurately by microscopic examination of the urine; that is, oxalate crystals in the urine indicate an oxalate stone, and uric acid crystals indicate uric acid stone. Is this generally true?*

Saul H. Kaplan, M.D., Miami Beach, Fla.

Answer.—In general, it has not been the experience of most urologists that an accurate determination of the composition of a kidney stone can be made by microscopic examination of the urine. Many oxalate stones are seen without oxalate crystals in the urine continuously. The same thing holds for uric acid stones. Most kidney stones are phosphatic in nature.

POST-TRAUMATIC PTOSIS

To the Editor:—*A 60-year-old man was hit by the horns of a cow on the left suborbital area and escaped with only slight injury of the soft tissues, but almost immediately he suffered from a complete ptosis of his left upper eyelid. There was no fracture, no headache, no pain in the eye, and no involvement of the mobility of the eyeball. Visual acuity, visual field, optic nerve head, and retinal vessels were normal. A neostigmine test showed negative results. It is known that isolated muscles innervated by the oculomotor nerve may be paralyzed either from brain stem involvement (since there are specific localizations within the oculomotor nucleus) or from involvement of the nerve itself. In this patient how can the isolated ptosis be explained?*

George C. Mavrantonis, M.D., Nicosia, Cyprus.

Answer.—Traumatic ptosis is a frequent sequel to a concussion of the orbital rim and may be due to damage of the levator tendon or injury to the palpebral branch of the oculomotor nerve. A force impinging in this area dissipates in the facial mass and the globe, orbital contents, and brain escape direct concussive injury, but the thin orbital roof usually gives way in the region of the superior orbital fissure. Such a fracture may occur without involvement of the superciliary arch. The causal injury may be so trivial that the patient is only momentarily dazed. Roentgenograms are of little help because of obscuration by denser surroundings. Since the ptosis from the injury described may recover spontaneously, a year should elapse before surgical intervention. In the meantime, symptomatic amelioration can be secured by a ptosis crutch attached to the spectacle frame.

XANTHOMA DIABETICORUM

To the Editor:—*In* The Journal, *Nov. 8, 1958, page 1423, a question was asked on the management of xanthoma diabeticorum. The consultant's advice was to the effect that nothing but surgical treatment was available. Xanthoma diabeticorum, in common with other forms of xanthomas, can be influenced favorably by manipulation of the quantity and quality of fats. Some persons are markedly improved with elimination of most fats from the diet, and others show significant or complete improvement with substitution of polyunsaturated fat for saturated fat in the diet. The latter means is to be preferred in a diabetic patient and should be tried before the former is resorted to. The type of diet which may be used for this purpose is outlined by Olson and others* (Am. J. Clin. Nutrition, **6**:632, *1958*).

Laurance W. Kinsell, M.D.
2701 14th Ave.
Oakland, Calif.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*Surgical excision only of early small lesions was suggested and this at a risk of recurrence. The present histopathological interpretation of this condition has been altered since its original designation as necrobiosis lipoidica diabeticorum. It might better be termed necrobiosis diabeticorum, dropping the lipoidica, since it is no longer considered a true xanthoma. In 80% of these patients there is some form of diabetic association, with a likely ensuing relationship in the rest. Histologically the lesion is essentially a necrobiosis of the collagen. Lipids are present in the tissue, but the disease is ordinarily unassociated with systemic involvement of lipid metabolism. One exception is in diabetics with lipemia which in some instances may be accompanied by hypercholesteremia. In view of this, it is unlikely to assume that the type of diet referred to would be of much value in producing resolution of these lesions. In the experience of most dermatologists, diet has not been worthwhile in this disease. It is pertinent, however, to suggest that the lesion of necrobiosis be definitely differentiated from true xanthomatous le-*

sion associated with systemic lipid disturbances. This may be achieved by means of clinical, pathological, and laboratory data.

OBESITY AND HYPOGONADISM

To the Editor:—*A question on obesity and hypogonadism appeared in* The Journal, *Aug. 23, 1958, page 2157, concerning an obese 14-year-old boy with a small penis, no male distribution of hair, and a basal metabolic rate of –19%. Several comments appear warranted. In the first place, the question is inadequate to allow a clear answer. No mention is made of presence or absence of testes, size of testes, presence of other secondary sex characteristics, skeletal proportions, or clinical features for or against hypothyroidism. These questions certainly require attention long before the patient is subjected to the expensive series of laboratory tests suggested in the answer. Moreover, certain important points are not considered in the answer. The wide range in age for the onset of puberty in normal boys must always be remembered. The odds are great that this boy does not have Froelich's syndrome. By implying that an endocrinopathy requiring treatment is present, the answer tends to perpetuate the common misconception concerning the fat boy in his early teens who has not yet entered puberty. The vast majority have no endocrinopathy and require no hormonal therapy.*

Philip Troen, M.D.
330 Brookline Ave.
Boston 15.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*The answer was prepared on the assumption that the question contained all of the available clinical facts. The writer's comment on the reply is traditionally acceptable. On the other hand, detailed study of obesity in boys with delayed sexual maturation will from time to time unearth evidence that endocrine or hypothalamic dysfunction is present and that these patients do not always represent one end of a distribution curve of normals. The therapy as outlined induces genital maturation, allays the concern of the parents and patient, and, in conjunction with calorie restriction and increased physical activity, aids in control of body weight.*

FIRST USE OF BLOOD TRANSFUSION

To the Editor:—*While one should hardly expect a complete history of blood transfusion in the Question and Answers section, the answer to the query in* The Journal, *Nov. 29, 1958, page 1834, about the historic facts concerning blood transfusion and the use of plasma is misleading. One can hardly dismiss the chief events in the development of blood transfusions if one mentions anyone but Richard Lower without mentioning Lindeman, who in 1912 used a syringe technique in place of the unsatisfactory vein-to-artery anastomosis, and Kimpton, who substituted paraffin-coated cylinders for syringes. Reference should be made to Hustin, who in 1914 laid the foundation for modern transfusion by the introduction of citrate as an anticoagulant. Lewisohn popularized this method by determining the proper dose of citrate and by using it enough times to establish the technique on a sufficiently firm footing to permit Pemberton to report in 1919 its exclusive use in the Mayo Clinic, at which time he had performed more than 1,000 transfusions by the use of citrate.*

With respect to plasma, the first comprehensive report was made in 1939 by Tatum, Elliott, and Nesset, who reported a complete method of obtaining satisfactory plasma and its use in 191 patients. This report may be said more correctly to have popularized the use of plasma than did the paper by Elliott published three years earlier. His paper only gave a method, which was rather an awkward one, of obtaining plasma, and there is no indication of his use of it. Elliott was still uncertain that it could be used indiscriminately with nonhomologous blood groups. If Strumia began the use of plasma in Bryn Mawr Hospital in 1927, as stated by the consultant, the date has no significance in priority, as he did not reveal that fact in the literature until 1940, although a photograph of a chart published by Nicholson in 1936 indicated the use of plasma at Bryn Mawr Hospital in March, 1934, in one patient. In 1941, Strumia and McGraw published the fact that they had used dried plasma, but they discarded it in favor of frozen or lyophilized plasma, a fact revealed in a paper by Strumia, Wagner, and Monoghan in 1940. At present, any plasma not preserved for at least six months at room temperature would be considered dangerous.

Finally, no report on the historic events in the use of plasma would be complete without reference to the farce of a few years ago when the irradiation of plasma was declared by leading authorities to be a safeguard against homologous serum hepatitis. Standard medical journals carried advertisements by commercial firms to the effect that such plasma was the complete answer to this problem. A definitive answer to it is still lacking, despite the fact that it appears to be generally accepted that plasma stored at room temperature for six months is safe. Perhaps it is.

Thomas B. Magath, M.D.
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